

ROAMS

(Review of All Medical Subjects)

A Concise Review for PGMEET

10th Edition

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- Concise review of all subjects.
- Special high yield points at the end of the book.
- Highlighted high yielding facts and mnemonics, useful charts.
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Abbreviations/Short forms Used in the Book

Ca	:	Carcinoma/Cancer	b/n or b/w	:	Between
~	:	denotes heading	Cl/f	:	Clinical features
D/to	:	due to	FA	:	Fatty Acid
↑	:	Increase, High	AD	:	Autosomal Dominant
n.or nv	:	Nerve	FFA	:	Free Fatty Acid
↓	:	Decrease , low	FTT	:	Failure to Thrive
D/g, Dx	:	Diagnosis	DM	:	Diabetes Mellitus
A/E	:	All except	CTD	:	Connective tissue disease
DOC	:	Drug of Choice	Cx	:	Cervix
R _x or T/t	:	Treatment	SCLC	:	Small cell lung carcinoma
Sx	:	Surgery	MN	:	Malnutrition
P/g	:	Prognosis	SM	:	Smooth muscle
IOC	:	Investigation of Choice	HCC	:	Hepato Cellular Carcinoma
P _x	:	Prophylaxis	BM	:	Bone marrow, basement membrane
TOC	:	Treatment of Choice	IOT	:	Intraocular Tension
C/c	:	Complication	HS	:	Hereditary Spherocytosis
Acc/ to	:	According to	HD	:	Hodgkin's Disease
C _T	:	Chemotherapy	BM	:	Bone marrow, basement membrane
Mc, m/c	:	Most Common	WT	:	Wilm's Tumour
R _T	:	Radiotherapy	HS	:	Hereditary Spherocytosis
Vs	:	Versus (= against)	NHL	:	Non-Hodgkin's Lymphoma
Supf.	:	Superficial	ICT	:	Intracranial Tension
Ds, d/s	:	Disease or Disease	SqCC	:	Squamous Cell Carcinoma
— —	:	Reaction block by, inhibited by	LN	:	Lymph node
Ms, m/s	:	Muscle	PBC	:	Primary Biliary Cirrhosis
B/L or b/L	:	Bilateral	MG	:	Myasthenia Gravis
Ipsi/L	:	Ipsilateral	MN	:	Malnutrition
U/L or u/L	:	Unilateral	WG	:	Wegner's Granulomatosis
Cont./L	:	Contralateral	ILD	:	Interstitial Lung Disease
A/w	:	Associated with	Ix	:	Indication
K/as	:	Known as	AR	:	Autosomal Recessive
V/s	:	Vessel			
Ad/E, ad/e	:	Adverse effects			
C/I	:	Contra indication			
A/w or a/w	:	Associated with			
M/m	:	Management			

BLOOD VESSELS (ARTERIES/VEINS)

Source of Hemorrhage/Bleeding in

Cause	Source
◦ Intradural hemorrhage (EDH)	Middle meningeal artery
◦ Sub dural hemorrhage (SDH)	Bridging/diploe veins
◦ Sub arachnoid hemorrhage (SAH)	Rupture of congenital Berry aneurysm
◦ Tennis ball injury to eye	Circulus iridis major
◦ Epistaxis	Submucous venous plexus, sphenopalatine artery
◦ During tonsillectomy	Paratonsillar veins, tonsillar and ascending palatine arteries
◦ Tracheostomy	Isthmus and inferior thyroid vein
◦ Hemoptysis, Bronchiectasis	Bronchial artery
◦ Gastric ulcer	Lt. gastric, splenic artery
◦ Duodenal ulcer	Gastroduodenal artery
◦ Hemorrhoids	Submucous venous plexus (formed by SRV + IRV)
◦ Retropubic prostatectomy	Dorsal venous plexus
◦ Hysterectomy	Internal iliac artery
◦ Menstruation	Spiral arteries

- Sphenopalatine artery is also k/as "artery of epistaxis"
- Longest branch from one of the lateral (or lenticular) striate branch of MCA artery is also k/as "Charcot's artery of cerebral hemorrhage"
- LAD is also k/as "widow maker" artery

Named arteries

- Heubner's Artery --- Recurrent branch of ACA
- Artery of Adam Kweicz --- Extends b/w T9 and T11
- Artery of Epistaxis --- Sphenopalatine artery

Preferred Artery for

- Cannulation - Radial a. and femoral a.
- Cerebral angiography (4 vessel angiography)
 - Both internal carotids + both vertebrals are used
 - Vertebral arteries are approached by percutaneous catheterization, which is done by passing a catheter through femoral artery
- Carotid angiography is performed by direct needle puncture of internal carotid arteries.
- Coronary angiography is done by passing a catheter through the **femoral artery** up into the aorta till the base of the ascending aorta. Judkin's method is a method of selective coronary artery catheterization utilizing the standard Seldinger technique through a percutaneous femoral artery.
- Coronary artery bypass graft (CABG) : Internal mammary graft is most favored f/b radial artery graft.

Preferred Veins for

- Injecting dye in fluorescein angiography --- Ante-cubital vein (peripheral vein)
- Venesection --- Long saphenous vein, Basilic vein (when CVP has to be monitored)
- For i/v injections --- Median cubital vein
- For TPN (i/v alimentation) --- Forearm veins.
- Injecting dye in phlebography --- Dorsal metatarsal vein
- Best vein for CABG graft --- Saphenous vein.

Other imp facts from arteries

- Quadrigeminal artery supplies tectum of midbrain.
- Deep optic artery is a central branch of middle cerebral artery (MCA)
- Blood supply of facial nerve is --- maxillary a.
- Stenosis of subclavian artery is common in --- First part.
- M/c site of aortic transection/ traumatic aortic rupture is aortic isthmus just distal to left subclavian a. (88-95%) [ligamentum arteriosum & brachiocephalic a. fixes aorta in this region]
- Splenic artery is a direct and largest branch of --- Coeliac trunk
- Right gastroepiploic artery is a branch of --- gastroduodenal artery.

- Ascent of horse shoe kidney is prevented by---Inferior mesenteric artery.
- Abberent obturator artery is a br. of → Inferior epigastric artery.
- Middle meningeal artery is a branch of → Maxillary artery (1st part).
- Nutrient artery of fibula is → Peroneal artery.
- Lt phrenic nerve is accompanied by → Internal thoracic artery.

Veins : Important Points

- Infection of angular vein can lead to thrombosis of cavernous sinus.
- Inferior jugular vein surface markings are : Ear lobule (upper end) to the medial end of clavicle (lower end).
- Vitelline veins give rise to → Portal vein, hepatic vein, sinusoids.
- Venous sinuses are sub-fascial in location.

ANATOMICAL FACTS

Parameter	Organ	Value
Capacity (volume) of	Stomach	1.1 - 2 L (30-50 mL in newborn)
	Gall bladder	30-50 mL
	Urinary bladder	250-500 mL
	Cranium	1400 cc

Weight of	Brain	1400 gm (1275 gm in females)
	Pituitary	0.5-0.6 gm
	Thyroid	20-40 gm
	Kidney	130-160 gm
	Adrenals	5-6 gms
	Testis	20-27 gm
	Prostate	15-20 gm

Length of	Spinal cord	45 cm
	Thoracic duct	45 cm
	Femur	45 cm
	Vas deferens	45 cm

Esophagus 25 cm

Ureter 25 cm

Optic nerve 4 cm

Inguinal canal, 4 cm

Anal canal

Female urethra 4 cm

ANATOMY BASICS

Large arteries, arterioles and capillaries

Distal aorta and Large Arteries	Arterioles	Capillaries
<ul style="list-style-type: none"> More elastic tissues & SM. Windkessel effect present 	<ul style="list-style-type: none"> Resistance vessels Seat of peripheral vascular resistance 	<ul style="list-style-type: none"> No SM, no contraction/dilatation. Continuous type present in muscles Fenestrated with discontinuous endothelium is found in liver, kidney.

- Highest mean velocity is seen in - aorta
- Windkessel vessels - distal portion of aorta and larger arteries (they have more recoil and elasticity)
- Maximum pressure drop occur in - small arteries and arterioles
- Resistance vessels - arterioles and small arteries
- Maximum total cross sectional area - capillaries (lowest velocity)
- Capacitance vessels - veins (contain 50% of circulating blood volume)
- Compliance is max^m in veins > aorta > arteries.
- Tunica media is found in all blood vessels except veins.
- Vasa vasorum is blood vessels plexus supplying blood vessels.

End arteries

Arteries which do not anastomose their neighbours.

- Central artery of Retina (Absolute end artery)
- Central branches of cerebral a.
- Vasa recta of mesenteric a.
- Arteries of spleen, liver, kidneys, lungs & metaphysis of long bone.

Capillaries

- Types : There are 3 main types of capillaries:

1. Continuous (M/c type)
2. Fenestrated
3. Sinusoidal

1. Continuous

- Endothelial cells provide an uninterrupted lining, and only allow small molecules, like water and ions to diffuse through **tight junctions** which leave gaps of unjoined membrane which are called intercellular clefts. Tight junctions can be further divided into two subtypes:

- a) Those with numerous transport vesicles that are primarily found in skeletal muscles, fingers, gonads, and skin.
- b) Those with few vesicles that are primarily found in the CNS. These capillaries are a constituent of the BBB.

2. Fenestrated -

- Fenestrated capillaries have pores in the endothelial cells (60-80 nm in diameter) that allow small molecules and limited amounts of protein to diffuse.
- Found in the renal glomerulus, vasa recta of renal medulla, endocrine glands, pancreas intestinal villi, and renal glomeruli.

3. Sinusoidal

- Sinusoidal capillaries are a special type of fenestrated capillaries (open pore/discontinuous type) that have larger openings (30-40 μ m in diameter) in the endothelium. Highly permeable d/to fenestrations.
- Sinusoids are found in the liver, lymphoid tissue, endocrine organs, and hematopoietic organs such as the bone marrow and the spleen. (but not in skeletal muscle)
- They may connect arteriole with venule (spleen, bone marrow), Venule with venule (liver)

Lymph Capillaries (Lymphatics)

- Have a discontinuous basement membrane. (*No visible fenestrations in lymphatic endothelium.*)
- Contain valves.
- Junction b/w endothelial cells are open. No tight intercellular connection.
- Lymphatics are NOT present in :- Brain, Eye, cornea, articular cartilage, Internal ear (CNS), Lens, epithelia, placenta, sclera bone marrow, splenic pulp, glottis, epidermis, (but +nt in dermis)*

Arteriovenous shunts (Shunt vessels)

- Rich A-V anastomosis are found in skin of nose, lips, ear lobule, g.i. mucosa, thyroid gland, palmar skin
- They are under autonomic control in skin. They regulate the regional blood flow, BP, temperature (*thermoregulation*).

Anastomosis

Arteries do not end always in capillaries, they unite with one another forming anastomosis. Sites of potential anastomosis are *coronaries, cortical arteries, and arteries around joints*.

Types and examples

1. *End- to- end* : labial branches of facial a., intercostal a., uterine/ ovarian arteries, arterial arcades in mesentery, arteries of greater and lesser curvature of stomach, palmar and plantar arches.
2. *Convergent* : Vertebral arteries to form basilar artery.
2. *Transverse* : B/w two ACA, b/w radial & ulnar arteries at wrist.

Veins which do not have muscular tissues

- Dural sinuses and pial veins
- Veins of maternal part of placenta
- Retinal veins
- Veins of spongy bones
- Venous spaces of erectile tissue of penis

Veins which do not have valves

- SVC and IVC
- Very small veins of diameter <2mm
- Hepatic, renal, ovarian, uterine, cerebral, emissary, pulmonary and umbilical veins

→ *Portal venous system is a valveless system*

→ *Portal circulation is seen in – liver and pituitary (hypophysis cerebri)*

→ *Counter current multiplier system is seen in – Kidney (LOH) and Vasa recta of testis.*

Veins containing oxygenated blood

- Pulmonary vein
- Umbilical veins

Arteries of the body which carry deoxygenated blood

- Pulmonary artery
- Umbilical artery

Arteries of the body where $P_{CO_2} > P_{O_2}$

- Pulmonary artery
- Gastric artery

Retroperitoneal Structures

- Head of pancreas, most of duodenum
- Aorta and IVC with branches
- Cisterna chyli, LN and vessels
- Kidneys, ureters, Suprarenal glands

→ Posterior surface of pancreas is related with termination of superior mesenteric vein and beginning of portal vein.

DANGEROUS AREA OF BODY

- *Danger area of scalp*: is the layer of **loose areolar tissue of scalp** because emissary veins open here which may transmit infection to venous sinuses.
- *Danger area of eye*: Ciliary body
- *Danger area of nose*: Olfactory area
- *Danger area of face*: Infection of the *lower part of nose and upper lip* may be transmitted to cavernous sinus by facial vein & its communications (superior ophthalmic vein and deep facial vein).

STRUCTURES FORMING VARIOUS BED

Bed	Structure
○ Tonsillar	Buccopharyngeal fascia Pharyngo-basilar fascia (by lower styloglossus) Sup. constrictor m/s, Palato-pharyngeus Glossopharyngeal n.
○ Stomach	Splenic artery Lt. crus, dome of diaphragm Lesser sac. Lt. Kidney (upper part) Lt. adrenal (upper medial), Pancreas (transversely), Spleen (upper lateral) Transverse mesocolon Splenic flexure of colon
○ Pancreatic	Splenic vein (<u>not a.</u>) Aorta & origin of sup. mesenteric a. Lt. renal vessels & ...Lt. kidney Lt. Suprarenal gland Lt. crus of diaphragm

BONES & JOINTS

Parts of a Long Bone

A long bone is composed of 4 parts. From centre to outwards these are:

- Diaphysis
- Metaphysis
- Epiphyseal growth plate (physis)
- Epiphysis

Diaphysis

Is elongated shaft of a long bone which ossifies from primary centre. TB and syphilis begin in the middle of shaft. It is the strongest portion of the bone. *Haversian system* is found in diaphysis.

Metaphysis

Epiphyseal end of a diaphysis. Richly supplied by **hair pin bends of arteries**. Area of greatest growth velocity in bone. Common site of **osteomyelitis** in children. Prone to traumatic necrosis, and **avascular necrosis**.

Epiphyseal plate/ Growth Plate (Physis)

It separates epiphysis from metaphysis. It is *cartilagenous* plate responsible for growth in length. It is the zone of endochondral ossification in an actively growing bone or the epiphyseal scar in a fully grown bone.

Epiphysis

End or tip of bone which ossify from secondary centre.

- Nutrient artery enters a long bone through **diaphysis** through an oblique canal & goes towards the growing ends. It supplies medullary cavity, cancellous bone in the shaft, and inner 2/3rd of cortex.
- Numerous metaphyseal and epiphyseal arteries supply the ends of bones.
- Growing ends of the bone are those where 2° centre appears first & fuses last. Proximal end of humerus tibia and fibula and distal end of radius, ulna and femur are growing end.
- A primary centre forms diaphysis and secondary centre forms epiphysis
- Bone grows in thickness by multiplication of cells in periosteum/ perichondrium

Types of Epiphysis

Epiphysis	Type/Role	Examples
1. Pressure	Articular	Head of femur, lower end of radius, condyles of tibia, head of humerus
2. Traction	Non-articular	Trochanters of femur, Tubercles (greater/lesser) of humerus, mastoid process
3. Aberrant	Not always present	Epiphysis at the head of 1st metacarpal
4. Atavistic	Phylogenetically an independent bone	Coracoid process of scapula, Os trigonum

→ 5 paired bones having pressure epiphyses at both ends are --- Humerus, radius, femur, tibia, fibula.

Appearance of Ossification centres

Ossification takes place by centre of ossification, which may be primary (1°) & secondary (2°). Primary centre appears before birth, usually during 7-8th week of IUL; the 2° centre appears after birth except of lower end of femur which appears just before birth (9th month).

Important Primary centres & age of appearance (fetal life)

- Femur shaft - 7th week
- Humerus, radius, ulna, tibia shaft - 8th week
- Ischium - 3rd month
- Pubis - 4th month
- Calcaneum - 5th month (3-5 months, or before viability)

After viability the 1° centres are given below

- Talus - 6-7th month
- Femur, lower end - 9 month (at/just before birth)
- Tibia, upper end - 9 month, at/just before birth

At birth in or in a full term newborn max^m 5 ossification centres are present. These are - lower end of femur, tibial tuberosity, calcaneus, talus and cuboid (all in the lower limb).

Appearance of 2° centres :

Ossification of **carpal bone** is important. It helps in determining bone age. Time of appearance of ossification centre for capitate is 2nd mo, hamate is end of 3rd mo, triquetral is 3rd yr, lunate is 4th yr, scaphoid/trapezium/trapezoid in 4-5 yrs, pisiform 10-12 yr.

Age	6 mo	1yr	2yr	3yr	4yr	5yr	6yr	12yr
No. of bones	0	2	2	3	4	4	7	8
		(H+C)		+ T	+ L	+ S, T, T		(All bone appear)

Ossification of bones/Bone formation

Intra-membranous	• Seen in cranial/ facial bones, clavicle & mandible
Endochondral	• Seen in most other bones. • Occurs in hyaline cartilage. • Hyaline model of bone is replaced by bone.

Membranous bones

Examples are facial bones, skull vault bones

Pneumatic bones

Bones contain air filled spaces. Examples are maxilla, ethmoid, sphenoid, frontal, mastoid /temporal [Mnemonic: MESF-M 1st 4 form para nasal sinuses].

Types of bone

Cancellous/Spongy / trabecular bones

- Present in flat bones/ end of long bones.
- Acc/to Wolf's law all trabeculae of cancellous bone are arranged along the line of stress.
- M/c affected by osteoporosis becoz they are more metabolically active than cortical bone

Cortical/compact bones

- Present in *shaft* of long bones (diaphysis).
- *Haversian canals* are present which runs longitudinally & cocentrically. These canals together with lamellae form osteon.
- *Volkmann's canal* are transverse or horizontal channels b/w Haversian canal and & medullary cavity.
- Spiral arrangement of fibres in osteon can withstand with severe twisting strains.

Sesamoid bones

- Develop in tendons. They are in the form of nodules embedded in tendons and joint capsules.
- They ossify after birth.
- No periosteum, no Haversian system, no medullary cavity.

- They are either articular (patella, pisiform) or non-articular (fabella).
- Function :** To minimize friction, to modify pressure/ direction of pull of a muscle, aids in maintaining local circulation.

Peculiarities of clavicle

- No medullary cavity.
- Only long bone which lies horizontally.
- 1st long bone to ossify.
- Ossifies from 2 primary centres.
- Only long bone to ossify in membrane.

CARTILAGE

- Specialized connective tissue
- Matrix is made up of glycosaminoglycans (hyaluronate, chondroitin sulphate), proteoglycans, CAM
- Fibrocartilage contains type 1 collagen, all other cartilages contain **type 2** collagen.
- Hyaline cartilage* is avascular, non-nervous elastic structure but tends to calcify in elderly. *Articular cartilage* is a type of hyaline cartilage which is devoid of nerves, vessels, peri-chondrium (so it has no regenerative power), and ossification/ calcification.

[Mnemonic : In articular cartilage No CalPROVeN]

- Water content ↓ es with ↑ ing age.
- Nourished by diffusion.
- Cartilage may become calcified. Tendency of calcification is seen in white fibrocartilage and hyaline cartilage.

→ Ligaments :

Fibrous bands which connects bone to bone. position and movements sensor

→ Tendon :

Connects muscle to bone.

- **Synovial membrane** lines whole of the interior of joint except articular surface covered by hyaline cartilage. It has poor nerve supply

→ Cartilage :

Have no vessels, no nerves (insensitive), no lymphatics. Contains anti-angiogenic factor.

- **Capsule & Ligaments :** *Rich nerve supply and blood supply. Acutely sensitive to pain/stretches (watch dog action of capsule to protect the joint from any strain)*

Cartilages : Types

1. Hyaline	<ul style="list-style-type: none"> Most abundant All cartilaginous bone are preformed in hyaline c~. Tendency to calcify after 40 yrs <ul style="list-style-type: none"> Embryonic, epiphyseal plate Articular, Arytenoid, Thyroid K(c)ostal Tracheal & bronchial Cartilage of nose & larynx [BLANKET]
2. Fibrocartilage	<ul style="list-style-type: none"> Menisci Intervertebral disc Intraarticular disc/Labrum (Glenoid labrum at shoulder & acetabular labrum at hip joints) Symphysis Acromioclavicular joint [MILIA]
3. Elastic	<ul style="list-style-type: none"> Cartilage in auricle/external ear, EAM, eustachian tube. Inlet of larynx, corniculate, cuneiform Epiglottis

→ *Endochondral ossification occurs in hyaline cartilage.*

→ *Fibroelastic cartilage is the only cartilage which contains collagen type 1, so it is n/c cartilage to ossify.*

JOINTS : Classification/ Types

Synovial joint

1. Hinge joint (Only flexion & extension possible)	Elbow, Ankle, interphalangeal joints.
2. Ellipsoid joint	Wrist, all MCPs, Atlanto-occipital.
3. Pivot (trochoid) jt	Sup & Inf. radioulnar Jt., Atlanto-axial.
4. Condylar / Bi-condylar jt.	Knee, TM joints of jaw.
5. Saddle jt.	Thumb (first CMC), sternoclavicular, calcaneocuboidal, incudo-malleus Jt.
6. Ball & Socket	Shoulder, hip, talo-calcaneo-navicular, incudo-stapedial Jt.

Fibrous joint

- Sutures are peculiar to skull

- Syndesmosis

Bones are connected by the interosseus ligament. Examples are *distal Tibiofibular Jt.*, Foot plate of stapes with oval window (tympanostapedial syndesmosis).

- Gomphosis (Peg & socket joint) : e.g. tooth in its socket (dentatoalveolar joint).

Cartilaginous joint

Joint is surrounded by *fibrous* capsule which is lined by synovial membrane. Classified into 2 acc/to cartilages covering articular surfaces:-

1. **Primary (Synchondrosis / hyaline cartilage joint)**
E.g. **growth plate** (b/w epiphysis and diaphysis of growing / long bones), sphenoid-occipital joint, first chondrosternal, costochondral joint (synostosis).
2. **Secondary (Symphyses or fibrocartilaginous joint)** -
Symphysis pubis, *manubriosternal joint*, intervertebral joints, sacrococcygeal joints (symphysis menti is not a true symphysis), acromioclavicular joint.

- In interpharyngeal joints, capsule is absent on dorsal sides
- Ear ossicles from outside to inside are **MIS** — malleus, incus, stapes. They are articulated with each other by synovial joints.
- Vomer-sphenoidal junction is syndylesis (It is a wedge and groove type of suture)
- Growth plate is an example of primary cartilaginous joint

Movements at Cervical (Neck) Joint

- Atlanto-occipital jt. : Flexion only
- Atlanto-axial jt. : Rotation of axis (29° - 54°)
- Other cervical jt. : Flexion & extension.

Shoulder (Glenohumeral) Joint

- Synovial joint of **ball and socket** variety
- Joint is *unstable* because head of humerus is 3 to 4 times larger than shallow glenoid cavity (4:1 disproportion)
- Glenoid labrum (ring of fibrocartilage) covers glenoid cavity.
- Most important factor in stability of joint is tone of different group of muscles > ligaments.

Factors protecting the joint

- **Rotator cuff** (musculotendinous cuff)
Formed by blending of 4 tendons **SITS** : Supraspinatus, Infraspinatus, Teres minor, and Subscapularis. Cuff is deficient inferiorly.
Of these, SIT Insert into greater tubercle of humerus and participate in S (abduction), IT (lateral rotation) & while subscapularis causes medial rotation & adduction of arm. [Teres major also causes medial rotation, adduction].
- **Long tendon of biceps** prevents upward displacement. It is intracapsular (invested in synovial membrane).
- **Coracoacromial ligament** ↑ surface for movement & protects superior aspect of joint

Movements at the shoulder the joint

- **Adduction:**
By *pectoralis major* + **LD**.
It is limited bec/of little surface of humerus is available for this movement.
- **Abduction:**
 - Abduction (1st 15°) is initiated by → **Supraspinatus**
 - But main abductor (15° to 90°) is → **Deltoid**.
 - Serratus anterior & trapezius assist in → overhead abduction (90° to 180°)

Humerus & scapula move in ratio of 2:1 (120° : 60°) throughout the abduction. Abduction fixates at 90° (because no further articular surface is available on humerus). 180° of abduction is possible only with lat. rotation of humerus.
- **Flexion:**
Clavicular head of pectoralis major + anterior fibres of deltoid.
- Shoulder is the *m/c* joint to dislocate and to undergo recurrent dislocations.
- Shoulder joint is the *m/c* joint which is surgically approached from the front.

Painful Arc Syndrome :

Pain in shoulder & upper arm during the mid range of gleno-humeral abduction. Caused by minor tear/ tendinitis/ calcification of **supraspinatus** tendon; subacromial bursitis, # of the greater tuberosity.

Acromioclavicular Joint

- Articulating surfaces are covered with fibrocartilage
- **Coracoclavicular ligament** consist of conoid and trapezoid ligaments. It is extremely strong and is principal factor in providing stability to joint and is responsible for transmitting weight of UL & scapula to clavicle.
- Movts are passive
 - **Elevation (shrugging of shoulder):** produced by upper fibres of Trapezius + Levator scapulae & rhomboids.
 - **Depression of scapula:** Lower fibers of trapezius + LD

Ankle (Talocrural) joint

- Synovial joint of hinge variety
- Deltoid ligament is attached to talocalcaneonavicular joint. It is a very strong triangular ligament and is crossed by tendons of tibialis posterior and FDL
- Dorsiflexion is produced mainly by ---Tibialis anterior; assisted by P.t.
- Plantar flexion is produced by gastrocnemius & soleus.
- *Sprains of the ankle* are almost always abduction sprains

of the **subtalar joint**.

- Inversion sprain leads to rupture of lateral collateral ligament.
- Eversion sprain leads to tearing of deltoid ligament
- In Pott's # subluxation commonly there is an isolated # of lateral malleolus

Joints of foot

- Inversion and eversion takes place at -- subtalar joint and TCN joint
- Inversion is produced by --- Tibialis anterior, tibialis posterior, FHL, FDL
- Eversion produced mainly by--peroneus longus & brevis; assisted by P.t., EDL, EHL
- Dorsiflexion is produced mainly by -- Tibialis anterior; assisted by P.t.
- **Deltoid ligament** is attached to TCN joint.
- **Triple arthrodesis** involves fusion of TN + TC+ CC joint.
- **Pes planus or flatfoot** is d/to --- Collapse of MLA (medial longitudinal arch)
- **Pes cavus is high arch foot (a/w claw foot)** is a/w unduly high MLA (There is dorsiflexion of MTP joints and plantar flexion of IT joints). C/b seen in poliomyelitis.
- **Bunion** is an adventitious bursa located over medial side of 1st MT head.

Medial longitudinal arch of the foot

- Formed by calcaneus + talus + navicular + cuneiform + medial 3 MT heads. TCN (talo-calcaneo-navicular) is the main joint. [MLA is NOT formed by cuboid and phalanges.]
- Talus is the keystone (head of talus forms summit)
- **Plantar calcaneonavicular/ Spring ligament** is important in maintaining MLA of the foot.

Lateral longitudinal arch of the foot

- Formed by calcaneus + cuboid + lateral 2 MT (4th and 5th) bones. Calcaneocuboid joint is the main joint.
- Calcaneum is the keystone. Arch is meant mainly for transmission of weight and thrust from ground.
- Plantar calcaneocuboid ligament is important in maintaining LLA of the foot.

→ *Transverse arch is maintained by tendon of peroneus longus and tibialis posterior.*

LYMPHATICS AND L/D

- Lymphatics usually accompany their blood vessels.
- Lymphatics are **not** found in brain, choroid, internal ear.
- Primary lymphoid organs are --- Thymus and bone marrow.
- Secondary lymphoid organs are --- Spleen, LN, tonsils, Peyer's patches, bone marrow.

L/D of Breast

• Sub areolar plexus of Sappy

Lies just beneath the areola. It drains breast, nipple and areola through deep lymphatics

- 75% lymph from breast ultimately goes to axillary LN. Majority of lymphatics from lateral quadrant accompany axillary tail and drain mainly into the **pectoral** group of LN (earliest affected). *Superolateral* quadrant of the breast is m/c affected in breast cancer.

Thoracic duct

Thoracic duct is the largest lymphatic channel in the body. It receives tributaries from---

In thorax

- Lt intercostal LN
- B/L descending thoracic trunk
- B/L ascending lumbar trunk
- Posterior mediastinal nodes

In neck

- Lt jugular lymph trunk
- Lt subclavian lymph trunk
- Lt bronchomediastinal lymph trunk

L/D of Esophagus

- *Cervical part* --- paratracheal & deep cervical LN
- *Thoracic part* --- posterior mediastinal LN
- *Abdominal part* --- paracardial group of left gastric LN

Lymphatics draining into deep cervical group of LN in neck

- **Tonsils** --- Jugulo-digastric LN.
- **Tongue** --- Jugulo-omohyoid
- **Thyroid and parotid** --- deep cervical LN

Lymphatics draining genital organs

- **Obturator LN** --- Cervix.
- **Pre-aortic** --- Fundus & upper part of uterus, fallopian tube, ovary, testis.
- **Para-aortic** --- Fallopian tube, ovary, testis

- **Common iliac** --- Receives afferent from external & internal iliac nodes and send their efferents to lateral aortic.

- L/D of Cx and uterus is to **external & internal iliac**, obturator, parametrial LN (but NOT to deep inguinal nodes)
- L/D of stomach is to **pancreatic & splenic nodes**.
- Lymph nodes which are usually benign-- occipital, posterior auricular, shotty inguinal LN

External iliac Nodes	Internal iliac Nodes
<ul style="list-style-type: none"> ● Deep layer of abd. wall (infraumbilical portion) ● Membranous urethra ● Prostate, base of UB ● Lower part of body of uterus ● Cx, vagina 	<ul style="list-style-type: none"> ● Structure which are usually s/ by internal iliac a. ● All pelvic viscera ● Anal canal above pectinate line ● Back of thigh, buttocks ● Deeper parts of perineum ● Prostatic, membranous urethra ● Whole female urethra ● Uterus, Cx, deep vagina
Superficial inguinal LN	Deep inguinal LN
<ul style="list-style-type: none"> ● Penis (except glans) ● Perianal subcutaneous tissue ● Anal canal below pectinate line ● Cornua of uterus ● Isthmic part of FT, Round ligament of uterus ● Superficial perineum ● Scrotum ● Vulva and inferior vagina ● Big toe 	<ul style="list-style-type: none"> ● Glans of penis (LN of Cloquet) ● Clitoris ● Lymphatics from lower extremities ● Penile (spongy) urethra

FASCIA

- **Superficial fascia of anterior abdominal wall:**
Fascia of Camper: Below umbilicus superf. fatty layer
Fascia of Scarpa: Below umbilicus deep membranous layer.
- **Colles' fascia:** Membranous layer (deep layer) of Superficial fascia of perineum.
- **Gallaudet fascia:** Deep fascia of perineum or its continuation.
- **Fascia lata:** Deep fascia of thigh
- **Buck's fascia:** Deep fascia of penis
- **Fascia of Denonvilliers:** Separates post. surface of prostate from rectum.
Also k/as **prostatoperitoneal membrane** or rectovesical fascia
- **Fascia of Waldeyer:** Condensation of pelvic fascia behind rectum. It attaches the lower part of rectal ampulla to sacrum and encloses sup. rectal vessels

- **Deep cervical fascia (fascia Colli)**

Deep fascia of the neck is condensed to form ---

- Investing layer** lies deep to platysma, forms collar
- Pretracheal layer** -- forms false capsule of thyroid gland to enclose it. It is thickened posteriorly to suspend ligament of Berry which causes movement of all thyroid swelling with deglutition.
- Prevertebral layer** -- continue as **axillary sheath**. (Fascia around the brachial plexus)
- Carotid sheath** -- condensation of the fibrous alveolar tissue around the main v/s of the neck i.e. common and internal carotid artery, IJV and vagus nerve.
- Buccopharyngeal fascia, Pharyngobasilar fascia.**

- **Hypogastric sheath** is a condensation of endopelvic fascia. Lateral ligament of bladder, uterosacral, and trans cervical ligaments are constituents of hypogastric sheath.
- **Fascia of Gerota** covers kidney and adrenal gland both. It has 2 layers -- anterior layer is k/as fascia of Toldt and posterior layer is called fascia of Zuckerkandl
- **Sibson's fascia** is suprapleural membrane which covers apex of lung
- **Fascia Bulbi or Tenon's capsule** is the fascial sheath of eyeball which extends from optic nerve to sclerocorneal junction.

SALIVARY GLANDS

	N/s	Duct	Histo
Parotid	Auriculotemporal br. of 5 + <i>Lesser petrosal br. of 9th</i> via otic ganglia	Stensen's duct ↓ Opens in vestibule of mouth opp. upper 2nd molar teeth Pierces buccinator	Purely serous acini
Sub mandibular (Sub-maxillary)	CT br. of 7 (Fibres from SSN)	Wharton's duct ↓ Opens in floor of mouth on summit of sub-lingual papilla (on each side of frenum)	Mixed (serous > mucinous)
Sublingual	CT br of 7	Bartholin duct Rivinus duct ↓ Wharton's duct/ directly in floor of mouth	Mixed but mainly mucinous acini
Lacrimal	Greater petrosal br. of facial nv. (Lacrimal nv.) via pterygopalatine ganglia	Lacrimal duct ↓ Directed downward, backward & laterally and opens in inf. meatus of nose [BLD]	

GANGLIA

Ganglia	Topographically related to nerve	Functionally related to -- nerve
Otic	Mandibular	<ul style="list-style-type: none"> • LSPN of 9th is preganglionic • Auriculotemporal br. of mandibular nv. is postganglionic & secretomotor to parotid gland
Sub-mandibular	Lingual	<ul style="list-style-type: none"> • Chorda tympani of 7
Spheno/Pterygo-palatine	Maxillary	<ul style="list-style-type: none"> • GSPN of 7 • Largest parasymp. ganglion, Hay fever ganglion • Secretomotor relay to lacrimal & nasal glands.

Geniculate ganglia

Fibres of GSPN arise here (in course of facial nv) but they relay to lacrimal gland via sphenopalatine ganglia.

Nodose ganglion

The **nodose ganglion** (ganglion of the trunk; inferior ganglion of vagus nerve) is cylindrical in form, 2.5 cm. in length. Visceral afferent in function carrying sensation of heart, larynx, lungs & alimentary tract from the pharynx to the trans. colon.

- **Ciliary ganglion** is located near the apex of orbit between the optic nerve and tendon of lateral rectus muscle. Post ganglionic fibres pass through short ciliary nerves - supplies sphincter pupillae and ciliaris muscle.
- **Superior cervical ganglion** is the largest ganglion of the neck.
- **Stellate ganglion** is formed by fusion of lower cervical & 1st thoracic ganglion. Damage to it can lead to **Horner's syndrome**.

NERVES

Named Nerves

- **Nervus intermedius of Wrisberg:**

Sensory component of facial nv (Carries taste sensation from ant 2/3 tongue & general sensation from external acoustic canal).

- **Nervous spinosus:**

Meningeal branch of mandibular nerve which passes through foramen spinosum.

- **Jacobson's nerve:**

Tympanic branch of 9th nv. It forms tympanic plexus in middle ear & enters the petrous bone through tympanic canaliculus.

- **Arnold's/Alderman's nerve:**

Auricular branch of vagus

- **Vidian nerve:**

Or nerve to pterygoid canal (br. of 7th) is formed in foramen lacerum by br. of GSPN containing parasympathetic secretomotor fibers + DPN (from cervical ganglia) carrying sympathetic vasoconstrictor fibres → Provides autonomic n/s to nasal sinuses (Nerve of Hay fever). **Vidian neurectomy** is done in *Vasomotor rhinitis*.

- **Nerve of Latarjet:**

Branch of main anterior gastric nerve. Cut in SV but preserved in HSV.

- **Criminal nerve of Grassi :**

Branch of posterior gastric nerve which supply fundus. It should be cut & dissected in highly selective vagotomy (HSV) to avoid recurrent peptic ulceration.

- **Nervi erigentes:**

Parasympathetic efferents $S_{2,3,4}$ are motor to detrusor muscle and inhibitory to bladder sphinctors

- **Nerve of Kuntz:**

Grey rami running upward from 2nd thoracic nerve.

→ **Trigeminal neuralgia (Tic Douloureux)** --- Is sharp, paroxysmal, u/L, excruciating pain in distribution of trigeminal nerve (usually V2 or V3)

→ **Sluder's neuralgia** --- It is the neuralgia of sphenopalatine ganglion. There is sharp nasal pain in the distribution of anterior ethmoidal nerve.

→ **Muscles s/by ansa cervicalis are** --- Infrahyoid, inferior belly of omohyoid, sternohyoid, sternothyroid

→ **N/s of skin around umbilicus** --- T_{10} ventral ramus.

→ **Greater auricular nerve supplies** --- skin over the angle of jaw (mandible & parotid area)

→ **Inferior alveolar nerve supplies** --- mylohyoid m/s, anterior belly of digastric, lower lip, incisors

→ **N/s of pinna is** --- mandibular nv.

→ **Superior alveolar nerves are branches of maxillary nerve**

Petrosal Nerves

- Greater superficial/ GSPN**
- First branch of facial nerve
 - Arises from geniculate ganglion
 - It joins DPN in foramen lacerum & forms nerve to pterygoid canal
 - Supplies lacrimal glands, nasal, mucous glands of Phx., palate

- Lesser superficial/ LSPN**
- Br. of 9 / tympanic plexus
 - Passes via otic ganglion through auriculotemporal br. of mandibular nerve
 - Supplies parotid.

- Deep /DPN**
- Br. of sympathetic plexus around ICA
 - Contains cervical symp fibre

- External / EPN**
- Inconstant br. of sympathetic plexus around middle meningeal a.

- Superior LN is related to superior thyroid artery
- RLN is closely related to inferior thyroid artery and medial surface of thyroid gland.
- The non-recurrent right recurrent LN is an anomaly which is a/w aberrant right subclavian artery.
- Rima glottidis is the narrowest part of larynx. A potential site of choking in fish bone obstruction. Main trunk ILN can be severed while removing fish bone from this area.
- Galen's anastomosis is a connection b/w SLN and RLN.

[For details of nerves and their branches students are advised to go through VDA's anatomy charts by the same author]

Distribution of Facial Nerve

- Branches within the facial canal

- GSPN
- CT (Chorda tympani)
- Nerve to stapedius

- Branches at its exit from the stylomastoid foramen

- Posterior auricular
- Posterior belly of digastric
- Nerve to stylohyoid m/s

- Terminal branches in face

- Temporal
- Zygomatic
- Buccal
- Marginal mandibular
- Cervical

- Anterior belly of digastric is s/by mandibular nerve

- Muscles of facial expression are s/by facial nerve, but levator palpebrae superioris by oculomotor nerve

- Facial nerve is supplied by maxillary artery.

- Greater superficial petrosal nerve (GSPN) is the first br. of facial nerve, it arises from geniculate ganglion.

- N/s of pyramidalis muscle ---subcostal nerve

- Pain of acute ethmoiditis is transmitted by nasociliary nerves

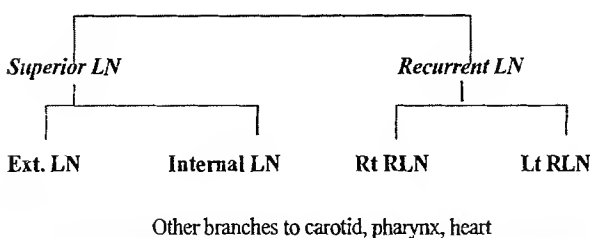
- Anterior and middle superior alveolar nerve is a branch of ---infra-orbital nerve, a branch of maxillary nerve

- Posterior superior alveolar nerve is a direct branch of ---maxillary nerve

Distribution of Vagus Nerve

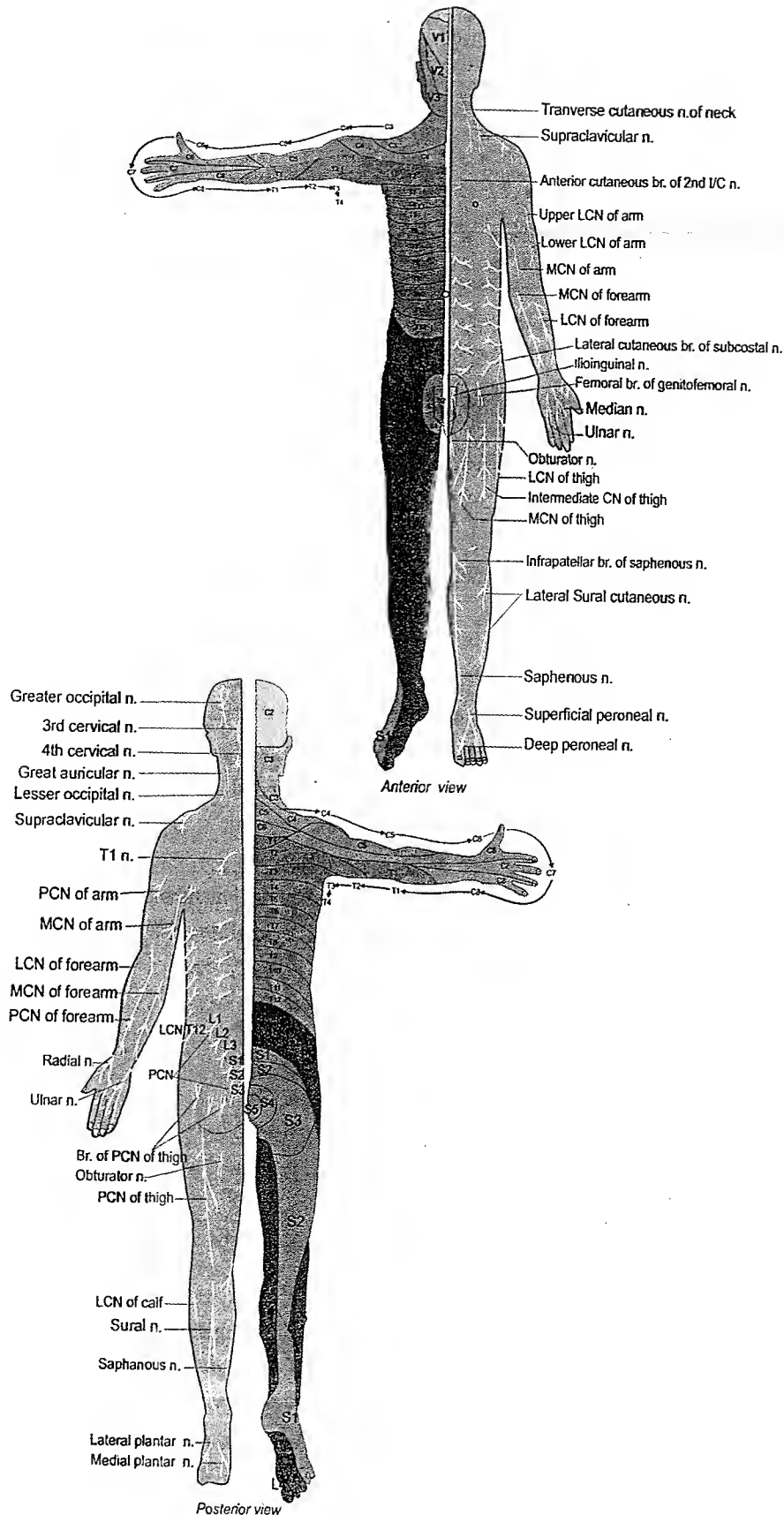
- In jugular foramen : Meningeal & auricular branch

- In neck (Laryngeal nerves)



Nerve	Supplies	Peculiarities
Ext LN	Cricothyroid	Accompany superior thyroid a.
Internal LN	Sensory to laryngeal mucosa above VC	Pierces thyrohyoid membrane
Rt RLN	All intrinsic m/s of Lx except crico, Sensory below VC, Branches to deep cardiac plexus, trachea, esophagus, inferior constrictor.	Arises from the vagus at the L/o Rt. subclavian a., hooks around it & then ascends up.
Lt. RLN	All intrinsic m/s of Lx except crico, Sensory below VC, Branches to deep cardiac plexus, trachea, esophagus, inferior constrictor.	Arises from the vagus in the mediastinum, at the L/o aortic arch, loops around it & then ascends into the neck

Sensory Distribution of Nerves



DERMATOMES AND CUTANEOUS NERVES OF BODY

3 Main Nerves of Forearm and their injuries

	Ulnar nerve	Median nerve	Radial nerve
Root value	C7-8 T1	C5C6C7 (Lateral root) C8T1 (Medial root)	C7,8 T1

Also k/as	Musician Nerve (deep br)	Labourer's nerve 'Eye of the hand'	Largest branch of brachial plexus
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Proximal lesions

Cause of Injury / lesion	At elbow # medial epicondyle, # lateral condyle humerus	At elbow Supracondylar # / lower end # humerus, application of tight tourniquet	In axilla Crutch palsy # disloc ⁿ upper end humerus, # lateral condyle humerus, (Ochsner clasp test +ve)
		At mid - forearm Pointing index (d/to FDS palsy)	

M/s paralysed	FCU, FDP, AdP	FCR	All the m/s s/by radial n., Supinator, Triceps Brachioradialis
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Result of lesion	Tardy or late ulnar n palsy, Valgus deformity of elbow, Cubital tunnel syndrome.	Pronator syndrome, Hand of Benediction deformity Simian hand / Ape thumb deformity is d/to flat thenar eminence (ulnar deviation of hand)	Wrist drop, Finger drop, Thumb drop
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Sensory loss	Medial 1½ fingers palmar surface	Palmar aspect + nail bed of lateral 3½ fingers	Dorsal aspect of lateral 3½ fingers
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Cl/f	Claw hand		
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Tests	Hook test or Froment's sign for deep branch of ulnar n.erve (Tests Add P) Card test	Pen test, Sign of Benediction (Inability to fully flex index and middle finger)	
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	Ulnar nerve	Median nerve	Radial nerve
Distal lesion	Injury at wrist	Injury at wrist	Injury in Radial/spiral groove/mid arm
Cause	Superficial injuries	Carpal tunnel syndrome # lower end radius, Dislocation of lunate/ semilunar	Saturday night palsy Compression on OT table, i/m injections, # shaft of humerus
M/s affected	FDP (medial ½)	AbP, OP	Intact triceps reflex and normal extension of elbow
Splints used	Knuckle Bender	---	Cock-up

- Median nerve is also called labourer's nerve because it controls coarse movements of hand.
- Ulnar nerve is also called musician's nerve (because it controls fine movements of hand)
- Ulnar nerve has got the worst and radial nerve has got the best prognosis in nerve repair.
- Weakness in powergrip is seen in # at spiral groove d/to paralysis of — ECRL
- At wrist, ulnar nerve is very superficial & therefore vulnerable to compression (Guyon's Canal Syndrome). Results in claw hand deformity.

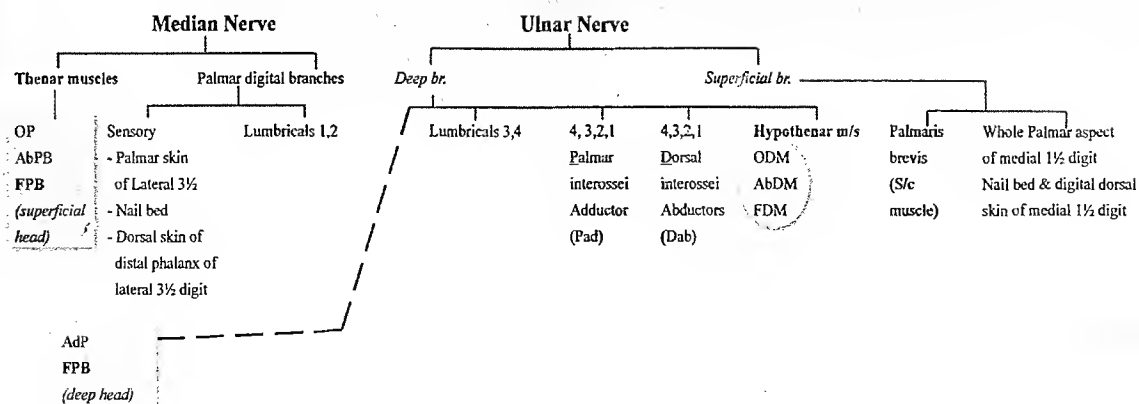
Clinical Tests of Median nerve lesion

- **Tinel's sign**
Percussion of flexor retinaculum results in tingling sense in the distribution of median nerve.
- **Phalen's test/maneuver**
Flexion or hyperextension of the wrist for one minute aggravates pain and parasthesia
- **Cuff compression test of Gilliatt and Wilson**
Pain and parasthesia aggravated when a BP cuff is applied to the arm & when compression is applied > Systolic BP.

Nerve Plexuses

- **Coeliac plexus (Solar plexus):**
Situated on the aorta and surrounds coeliac trunk and root of SMA. Plexus is anteromedial to sympathetic chain
- **Superior hypogastric plexus :**
Lies in front of bifurcation of aorta
- **Inferior hypogastric plexus :**
Contains pelvic splanchnic nerves

N/s of Hand

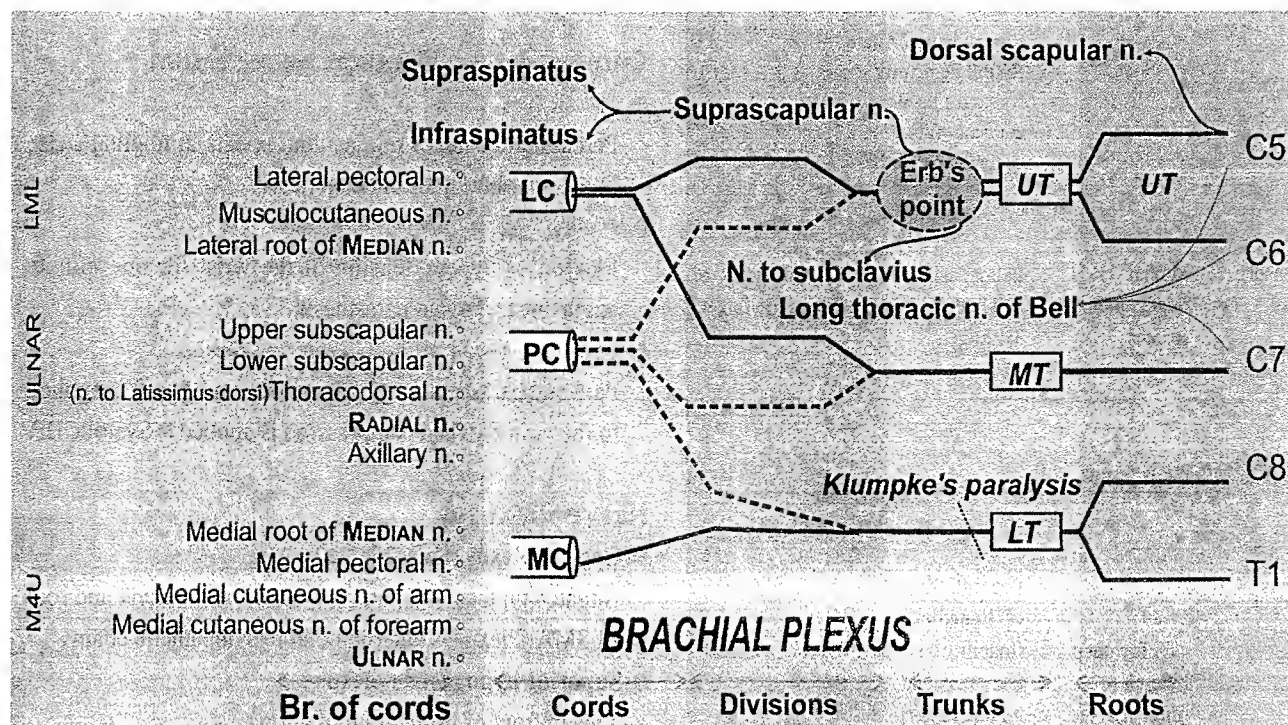


Sensory supply

- **Median nv** - Palmar skin of lateral 3½ digit, nail bed & dorsal skin of distal phalanx of lateral 3½ digit.
- **Ulnar nv** - Dorsum of skin of medial 1½ digit, Palmar aspect of medial 1½ digits. Nail bed & dorsal skin over distal phalanges of medial 1½ digits.
- **Radial nv** - Skin of dorsum of lateral 3½ digits (excluding nail bed & skin of lateral 2/3rd of dorsum of hand).

- All small muscles of hand (thenar, hypothenar, interossei and lumbricals) are supplied by C8, T1 nerve roots
- All thenar muscles (FPB, OP, AbP) are s/by median nerve except adductor pollicis which is s/by ulnar nerve
- Thumb is used to test all muscles of hand

Brachial Plexus



Nerves in relation to humerus

Nerve	Root value	Related to
Axillary	C5,6	Surgical neck humerus
Musculocutaneous	C5,6,7	
Radial	C5,6, 7,8T1	Mid shaft humerus (spiral groove)
Median	C5,6, 7,8T1	
Ulnar	C8T1	Groove behind medial epicondyle

Axillary nerve (C5- C6)

- Injured in # surgical neck (upper end of shaft) of humerus, anterior dislocation of shoulder, and # head of humerus.
- Deltoid m/s paralysis → Loss of rounded contour of shoulder (**Flat shoulder**), poor abduction.
- Paralysis of teres minor & sensory loss over lower half of deltoid is seen.

- Long thoracic nerve or nerve to serratus anterior is also called—Nerve of Bell
- Anatomical neck of humerus is the articular margin b/w head & shaft.
- 3 branches of radial nerve in spiral groove are —br. to lateral head of triceps, medial head of triceps, and anconeus.

Musculocutaneous nerve (C5,6,7)

- Nerve of anterior compartment of arm
- Branch of lateral cord of brachial plexus
- It supplies : BBC --- Biceps brachii, Brachialis, and Coracobrachialis
- It continues as lateral cutaneous nerve of forearm
- Lesion results in
 - Loss of supination, biceps jerk, loss of sensation over lateral border of forearm.
 - ↓ flexion at elbow.

N/s of Hip joint

Acc/ to Hilton's law hip joint is supplied by 3 nerves of pelvic girdle & LL

1. Femoral nv via nerve to rectus femoris ,
2. Sciatic nv via nv to quadratus femoris
3. Ant. division of obturator nv

Cranial Nerves (CN) and their peculiarities

• Olfactory

Olfactory pathway to the highest cortical centre is ipsilateral. All other sensory paths have crossed cortical representation

• Trochlear

Only CN to emerge from dorsal aspect of brainstem. Longest intracranial course. Motor n.

Only CN to undergo complete internal decussation before emerging, supplies contralateral SO m/s.

• Trigeminal

Largest nerve. Passes through Meckel's cave.

• Vagus

Longest cranial nerve in body, most extensive distribution

• Facial

M/c cranial nerve to be paralysed, longest course through bony canal of skull

• Abducent

M/c cranial nerve affected in raised ICT, cerebral aneurysm (along with oculomotor)

- 3rd & 4th cranial nerves attach to midbrain, 5th to pons, 6th, 7th, 8th to junction of pons and medulla, 9th, 10th, 11th, 12th attach to medulla.

CN nuclei & their functional columns

Sensory

- SSA — CN 2, 8
- SVA (BA) — CN 1, 7, 9, 10

Motor

• Somatic efferent column

CN 3, 4, 6, 11s, 12 (Oculomotor, trochlear, abducent, hypoglossal, spinal accessory)

• BE (SVE)

CN 5, 7, 9, 10, cranial accessory

→ Tractus solitarius is related to gustation.

→ NTS give rise to cranial nerves Nine, Ten, Seven (9, 10, 7).

SOME IMPORTANT MONONEUROPATHIES

Nerve	Origin (Spinal segment)	Clf	Cause/remark
Supra-scapular	C ₅ C ₆	lateral rotation of scapula ↓	Injured near suprascapular notch
Long thoracic n. (Nerve of Bell)	C ₅ C ₇	Paralysis of serratus anterior ↓ Winging of scapula	Loss of overhead abduction also seen
Radial n.	C ₅ -T ₁	Wrist drop (Loss of thumb & finger extension) Cheiralgia parasthetica (Paresthesia & sensory loss over thumb d/to lesion of dorsal digital branches)	<i>Saturday night palsy</i> (acute compression), injured in spiral groove
Post. interosseous br. of radial nerve	C ₇ C ₈	Finger drop relative sparing of wrist	Finger & thumb extensors paralyzed
Ulnar n.	C ₈ T ₁	Extended MCP + flexed IP joints of fingers ↓ Claw hand Cubital tunnel syndrome	Paralysis of Lumbricals, more marked in low ulnar nv. palsy. Deep terminal br. is purely motor which may be compressed in Guyon's canal (pisohammar canal) in injury near elbow
Median n.	C ₆ - T ₁	Carpal tunnel syndrome	In acromegaly, amyloidosis, DM, hypothyroidism
Anterior interosseous br. of median nerve	C ₆ - T ₁	Loss of pinch grip	Paresis of flexion of terminal phalanx, index and middle finger
Femoral n.	L ₂₋₄	Knee buckling Quadriceps femoris & Iliopsoas paralyzed Absent knee jerk Weakness/atrophy of anterior thigh n/s	Proximal to inguinal ligament
Lateral cutaneous nerve (LCN) of thigh, a br. of femoral nerve	L _{2,3}	Meralgia paresthetica Dysesthetic hyperpathia of lateral thigh	Normal Knee jerk Tingling, numbness of skin

PCN of thigh	S1-S3	Sensory loss over posterior midline of thigh	Sacral plexus injury
Obturator	L ₃ L ₄	Loss of adduction of hip, Sensory deficit over medial thigh.	
Sciatic n.	L ₄ - S ₂	Flail foot, Severe leg/hamstring weakness	Near sciatic notch
Deen peroneal n. (Ant. tibial nv.)	L ₄ - S ₂	Foot drop (loss of dorsiflexion of toes and eversion of foot) ↓ Inability to stand on heel	Neck of fibula
Post. tibial n.	L ₅ - S ₂	Tarsal tunnel syndrome	Medial malleolus in tarsal tunnel, in RA

LIGAMENTS, TENDONS, TRIANGLES, ANGLES

Ligaments

Fibrous bands which connects bone to bone

- **Deltoid ligament** is attached to talocalcaneonavicular (TCN) joint and tibia. It is composed of tibioalcaneal ligament & tibionavicular ligament
- **Coracoclavicular Ligament** is extremely strong & is the main factor in providing stability to acromioclavicular joint.
- **Lacunar ligament** is a crescent shaped extension of fibres at the medial end of the inguinal ligament
- **Cooper's (Pectineal) ligament** is a extension of fibres from lacunar ligament along pecten pubis of pelvic brim
- **Gastrosplenic ligament** contains short gastric vessels.
- **Leino-renal ligament** contains splenic vessels & tail of pancreas.
- **Phrenico-colic ligament** supports anterior end of spleen & prevents its downward displacement.
- **Struthers' ligament** is an inconstant ligament that extends b/w the shaft of the humerus and the medial epicondyle of the humerus
- **Pubourethral ligament** found in female
- **Puboprostatic ligament** is found in male

- **Ilio-femoral ligament (Ligament of Bgelow)** is one of the strongest ligament of the body
- **Spring ligament (plantar calcaneonavicular ligament)** is a strong ligament which supports TCN joint (anterior subtalar joint) from ventromedial side

TENDONS

Connects muscle to bone

- **Tendon of Todaro:** It forms boundary of Koch's triangle
- **Conjoint tendon:** Is formed by fusion of lower fibres of IO+ TA. Also k/as *falx inguinalis*

- *Tendocalcaneus is the thickest and strongest tendon of the body*
- *FHL tendon passes below the sustenticulum tali*
- *Pes anserinus is combined tendinous insertion of sartorius, gracilis and semitendinosus*

TRIANGLES (Δ)

- **Δ of Doom**

Bordered by the vas deferens medially, gonadal vessels laterally, and peritoneal edge posteriorly, contains the external iliac vessels, the deep circumflex iliac vein, the femoral nerve, and the genital branch of the genitofemoral nerve.

- **Δ of auscultation**

Bounded by 2 muscles and scapula.

Superiorly – Trapezius,

Inferiorly – Latissimus dorsi and

Laterally – medial wall of Scapula

Rib 7 and Rhomboideus major lie in the floor of Δ

- **Koch's Δ**

Is an important landmark for **AV node**.

Boundaries includes ---- Tendon of Todaro, Coronary sinus, and Base or septal leaflet ring of Tricuspid valve.

- **Calot's Δ**

Is bounded by ---- cystic duct (right), common hepatic duct (left) & porta hepatis (forms base). Contains cystic artery, right hepatic artery, accessory right hepatic artery and accessory bile ducts.

Is an important landmark during *cholecystectomy*

- **Trautmann's Δ**

Bounded by ---- bony labyrinth (anteriorly), Sigmoid sinus (posteriorly) & Superior petrosal sinus or dura (above)

- **Lumbar Δ of Petit**

Potential site for **lumbar hernia**

Bounded by lateral border of LD (medially), Posterior border of external oblique (posteriorly) & Iliac crest which forms the base (Inferiorly)

- **Deltopectoral Δ**

Infraclavicular fossa.

ANGLES

- **Renal angle:** Formed b/w 12th rib and erector spinae.
- **Sternal angle:** Second costal cartilage joins to sternum at this level (also k/as angle of Louis)
- **Citelli's angle:** also k/as Sinodural angle, situated b/n the sigmoid sinus and middle fossa dura plate.
- **Solid angle:** Area where three bony semicircular canals meet.
- **Alpha angle:** The angle between the visual and the optic axes as they cross at the nodal point of the eye.
- **Kappa angle:** The angle formed by pupillary axis and visual axis at the pupil.
- **Cobb angle:** Angle measuring scoliosis on a radiograph.
- **Angle of inclination :** Angle formed by intersecting femoral neck angle (NA) with axis drawn through shaft of femur (SA) This angle normally varies b/w 90° and 160°, with an average of 135°.
- **Urethrovesical angle** is the ∠ b/w the female urethra and the posterior vesical wall, normally about 90°-100° narrowing of this ∠ in cystocoele predisposes to stress urinary incontinence.
- **Aperture / angle of female pubic arch/subpubic angle** is 80°-85° in female & 50°-60° in male.
- **Greater sciatic notch** is wider in female (75°) than male (60°).
- **Subpubic angle** is 80°-100° in gynaecoid pelvis.

MUSCLES

- **Multipennate** muscle is a muscle in which the fiber bundles converge to several tendons.
- **Amyoplasia** is congenital absence of a m/s. Seen in Poland syndrome (undeveloped pectoralis m/s).
- **Multiunit smooth m/s** are seen in iris.
- **Quadriceps femoris** is a composite **group** of m/s.
- **Inf. Oblique** is only extrinsic m/s of eye, which does not take origin from Annulus of Zinn. (orbit)

Subcutaneous muscles

Platysma, Dartos, Palmaris brevis, Corrugator cutis ani, Subareolar muscles of nipple, muscles of scalp.

M/s with dual nerve supply

M/s	Nerve ₁	Nerve ₂
Brachialis	Musculocutaneous is motor	Radial n. is proprioceptive
Adductor magnus	Posterior division of obturator n. (adductor part)	Tibial part of sciatic n. (hamstring part)
Pectineus	Femoral nerve (ant. fibres)	Obturator n. (post. fibres)
Digastric	Mylohyoid br. of mandibular n. (ant. belly)	Facial n. (post. belly)
FPB	Median (superficial head)	Ulnar (deep head)
FDP	Anterior interosseus br. of Median (lateral half)	Ulnar (medial half)
Biceps femoris	tibial division of sciatic n. (long head)	Common fibular n. (short head)

Composite (Hybrid) Muscles

Muscle supplied by two different motor nerves with different root values is called a composite or hybrid muscle. Examples are:

1. Adductor magnus
2. Flexor digitorum profundus
3. Pectoralis major

Cruciate Muscles

Muscles in which fasciculi are crossed

1. Sternocleidomastoid
2. Masseter
3. Adductor magnus
4. Oblique arytenoid muscles

M/s of Mastication

- Temporalis: Retraction
- Lat. pterygoid: Depressor (side to side movt, yawning)
- Medial pterygoid: Elevator
- Masseter: Elevator (Tonic spasm e.g. in tetanus causes lock jaw)

- Protrusion & Lateral (side to side) movts by medial and lateral pterygoid.
- Depressor of Mandible (opening of Jaw) : Digastric, Geniohyoid, mylohyoid, Lat. pterygoid.
- Opening of Auditory tube : When levator palati contracts.

Digastric Muscles

M/s in which there are 2 bellies with two different origins

1. Occipitofrontalis (Occipital & frontal belly)
2. Omohyoid (Anterior & posterior belly)
3. M/s fibres in ligament of Treitz
4. Digastric (Anterior & posterior belly)

Named Muscles

- Boxer's m/s → Serratus anterior
- M/s of marriage → Medial rectus
- M/s of honeymoon → Sartorius
- Swing m/s → Pronatus quadratus
- Climbing m/s → Latissimus dorsi
- M/s of divorce → Lateral rectus
- M/s of rape or anti rape → Gracilis (gracilius)
- Tailor m/s → Sartorius
- Red m/s → Postural muscles
- White m/s → Extra ocular m/s
- Spurt m/s → Brachialis
- Shunt m/s → Brachioradialis
- M/s used in Grinning (Risorius), Smiling /laughing: (zygomaticus major.) and in Grief: (Depressor anguli oris)

→ Genioglossus is called safety muscle of tongue. (Fan shaped and forms main bulk of tongue)

→ Posterior cricoarytenoid is called safety muscles of larynx (causes abduction of vocal cords)

→ Mylohyoid forms Buccal diaphragm.

Muscles of

1. **Inspiration** : Diaphragm is major ms. > ext. IC > scalene, sternomastoid (Accessory muscles)
2. **Expiration** :- Mainly passive > m/s of ant abdominal wall (Rectus abdominis) > Internal IC

Guy Ropes

3 Muscles are inserted into the upper part of medial surface of tibia from 3 different compartment of thigh

1. Sartorius - belongs to ant. compartment (n/s - nv to ilium, br. of femoral nv)
2. Gracilis - belong to medial compartment (n/s - nv of pubis, br. of obturator nv)
3. Semitendinosus - belongs to post. compt. (n/s - nv of ischium, br. of sciatic nv)

M/s of 3 compartments of thigh/leg

	Compartment	Muscles	Nerve
Thigh	Medial / Adductor	Adductors - longus, brevis, magnus, gracilis, pectineus	Obturator
	Anterior/ Extensor	Sartorius, quadriceps femoris (3 vasti & rectus femoris)	Femoral
	Posterior/ Flexor	Hamstrings (SM, ST, long head of biceps femoris, ischial head of adductor magnus)	Tibial part of sciatic
Leg	Anterior	Tibialis anterior, EHL, EDL, Peroneus tertius	Ant. tibial (deep peroneal)
	Lateral / Peroneal	Peroneus longus & brevis	Superficial peroneal
	Posterior	Superficial muscles (gastrocnemius, Soleus, plantaris) Deep muscles (popliteus, FDL, FHL, tibialis posterior)	Tibial nerve (S ₁ S ₂) (also called post. tibial n)

- All muscles of anterior compartment of thigh cause extension of knee except sartorius which causes flexion
- Major factor in preventing forward leaning of trunk during walking is gluteus maximus m/s. It helps in rising from sitting position and is the chief extensor at hip joint.
- Flexion of Trunk (Lumbar spine) is carried by : Rectus Abdominis.
- Lat flexion of trunk : ipsi/L Ext. Oblique + Cont./L I.O
- Rotation of trunk : Combined action of EO+IO.

- **Quadriceps femoris** : Composed of rectus femoris & 3 vasti, it is chief extensor at knee joint and supplied by femoral nv.
- **Quadratus femoris** : Powerful lateral rotator of thigh and supplied by L5, S1 (from sacral plexus)
- **Biceps femoris** : When knee is semi flexed - Biceps femoris is a lateral rotator of leg and S.M. & S.T. are medial rotator of leg. When hip is extended Biceps femoris is a lateral rotator of thigh.

○ Attachment on iliotibial tract :-

Tensor fascia lata,

Gluteus maximus, Vastus lateralis (some part)

Iliotibial tract stabilizes the knee both in extension and partial flexion. In leaning forward it is main support of knee.

○ Attachments on Sustentaculum tali

1. Slip of tibialis posterior tendon
 2. Plantar calcaneo-navicular (Spring) ligament
 3. Medial calcaneal ligament.
 4. Superficial fibres of deltoid ligament.
- FHL tendon passes below S~

○ Lateral rotators of thigh

Quadratus femoris, piriformis, obturator internus, gemelli are main m/s
Others are gluteus maximus, and sartorius

- Tibial collateral ligament is degenerated tendon of Adductor magnus.
- Fibular collateral ligament is degenerated tendon of peroneus longus.
- Oblique popliteal ligament is derived from semimembranosus.
- Palmaris longus muscle is a degenerating muscle it is absent in 10% of subjects.

M/s in relation to scapula

- M/s arising from tip of coracoid process --- Short head of biceps, coracobrachialis, pectoralis minor
- Retractor of scapula are --- Trapezius, rhomboideus major and minor
- Trapezius muscle steadies scapula:
 - Its upper fibre + Levator scapulae elevate scapula (shrugging)
 - Middle fibres + Rhomboideus retract scapula
 - Upper & Lower + Serratus anterior involved in abduction of arm >90°
- Difficulty in shrugging of shoulder is seen in injury to spinal accessory nerve & in posterior Δ incision d/to sternocleidomastoid paralysis.

Upper Limb Muscles

- **Lumbricals**: arise from FDP and cause flexion at MCP + extension at IP joints (lesion causes claw hand).
- **Radial (lateral) collateral ligament**
Fan-shaped ligament which gives origin to supinator, ECR brevis.
- **Ulnar (medial) collateral ligament**
Triangular-shaped ligament which gives origin to flexor DS. Related to ulnar nerve, flexor C U & triceps.

ATTACHMENT OVER BONES

Part of bone	M/s attachment	Ligament/ membrane attached to it
Humerus, upper end	Subscapularis	
Humerus, medial epicondyle	Common flexor origin	
Humerus, lateral epicondyle	Common extensor origin	
Radial tuberosity	Biceps brachii	
Ulnar tuberosity	Brachialis	
Styloid process of radius	Brachioradialis insertion	-
Styloid process of ulna		Ulnar collateral ligament
Pisiform bone	Flexor CU	Pisohammarate ligament
Rib, 1st	Scalenus anterior, Scalenus medius	Suprapleural membrane
Rib, 2nd	Scalenus posterior	
ASIS	Sartorius	Lateral end of inguinal ligament
Femur, lesser trochanter,	Psoas major, iliacus	
Femur, greater trochanter	Gluteus medius, minimus, All lateral rotators of thigh except quadratus	

Structures Piercing

- Musculocutaneous nerve pierces --- Coracobrachialis m/s
- Posterior interosseous nerve pierces --- Supinator.
- Median nerve pierces --- Pronator teres.
- Internal laryngeal nerve (ILN) pierces --- Thyroid membrane.
- Parotid duct pierces --- Buccinator.
- Structure piercing clavipectoral fascia --- Thoracoacromial vessels, Lateral pectoral nerve & lymphatics
- Cephalic vein [Mn: TLC]

STRUCTURES PASSING THROUGH FORAMINA/CONTENTS OF

• Structures passing through foramina in orbit

Superior orbital fissure (SOF)	Upper part	1. CN 4, 5 (Frontal, nasal, lacrimal br) 2. Superior ophthalmic vein 3. Recurrent meningeal branch of ophthalmic a. Lower border provides attachment to common tendinous ring of Zinn.
	Middle part	Nasociliary n. CN 3 (divisions), 6
	Lower part	Inferior ophthalmic vein Sympathetic plexus
Inferior orbital fissure (IOF) [ZIME]		1. Zygomatic nerve 2. Infra-orbital vessels 3. Maxillary nerve 4. Emissary vein
Optic canal		- Optic nerve, sympathetic nerves - Ophthalmic a. - CRV

- **Optic foramen** --- is situated between Lesser wing and Body of sphenoid (LB)
- **Choroid fissure of eye** --- Hyaloid artery
- **Sinus of Morgagni**
(Semilunar space b/w base of skull & sup. constrictor)
 - Auditory tube
 - Levator palati
 - Ascending palatine a. [M-A-L-A]
- Between superior and middle constrictor :
 - Stylopharyngeus m/s its nerve (CN9)
- **Carotid sheath**
 - Internal jugular vein,
 - Common carotid artery (ICA in upper part)
 - Vagus n. [Note: Sympathetic trunk is outside]
- **Carotid canal** : ICA
- **Mandibular canal/foramen** : Inf. alveolar nerve/vessels.
- **Incisive foramen**: Greater palatine v/s & nasopalatine n.
- **Foramen rotundum** --- Maxillary nerve
- **Foramen ovale**
 - Mandibular nerve
 - Accessory meningeal artery
 - Lesser petrosal nerve
 - Emissary vein. [Ovale - MALE]
- **Foramen spinosum**
 - Middle meningeal a. & v.
 - Emissary vein
 - Nervous spinosus (MENINGEAL branch of mandibular nerve) [MEN]

- **Foramen lacerum** - B/w petrous & sphenoid. Lower part is filled with cartilage while upper part transmits ICA.
- **Hypoglossal canal**
 - Hypoglossal n. & its meningeal branch
 - Meningeal branch of ascending pharyngeal artery.
 - Emissary vein
- **Jugular foramen**
 - Ant part : Inferior petrosal sinus
 - Middle part : CN 9, 10, 11 + Meningeal br. of ascending pharyngeal artery.
 - Posterior part: - Occipital a. + IJV, emissary vein
[Note : CN 12 passes through hypoglossal canal]
- **Intervertebral foramen**
 - Radicular a.
 - Spinal nerves
- **Structures in relation to cavernous sinus**

Cavernous sinus (CS)	Structures
Structures passing through the CS (Contents of CS)	CN 3,4, V ₁ , V ₂ , 6, ICA
Structures traversing lateral wall of CS (above downwards)	CN 3,4, V ₁ , V ₂
Structures piercing roof of CS	CN 3,4, ICA

- **Foramen magnum transmits**
 - Narrow ant part : Apical ligament of dens, vertical band of cruciate lig, membrana tectoria
 - Wider post part : 4th part of vertebral a., spinal accessory n., symp plexus, spinal vessels
 - Sub arachnoid space : lowest part of medulla oblongata, 3 meninges,
- **Sacral canal**
 - Cauda equina (nerve fibres)
 - Filum terminale (end of spinal cord)
 - Spinal meninges (dura, arachnoid)

So lower sacral nerve pierce the dura, arachnoid at S₂ level
- **Structures emerging at sacral hiatus**
S₅, A pair of coccygeal nerve, Filum terminale
- **Structures passing through lesser sciatic foramen**
 - Pudendal nerve
 - Int. pudendal vessels
 - Nerve and Tendon of Obturator internus [P I N T]

Of these P I N passes through Greater sciatic foramen
PI passes through pudendal canal

- Foramen transversarium is present in the transverse process of cervical vertebrae. It transmits vertebral vessels & sympathetic plexus (C1-C6)
- Dorello canal is an opening in cavernous sinus and transmits abducent nerve.
- Sternberg's canal is located antero-medial to foramen rotundum & is d/to incomplete fusion of greater wing of sphenoid with the pre sphenoid. A/w spontaneous CSF leaks & meningocoele
- Foramen of Vesalius (or emissary sphenoidal foramen) transmits emissary vein.
- Wide neural foramina are seen in ---Neurofibromatosis

HEAD AND NECK

Parts of Brain

Part	Division	Structures
Forebrain (Prosencephalon)	Telencephalon	Cerebrum
	Diencephalon (Thalamian cephalon)	Thalamus, hypo, meta, epi thalami
Midbrain (Mesencephalon)		Crus cerebri, substantia nigra
		Tegmen
Hindbrain (Rhombencephalon)	Myelencephalon	Medulla
	Metencephalon	Pons, cerebellum

- Metathalamus is made up of medial & lateral geniculate bodies (MGB+LGB).
- Epithalamus contain pineal body, Habenular trigone, post commissure, optic cup
- Lateral ventricles develop from telencephalon (and form cavity of cerebrum)
- 3rd ventricle develops from diencephalon
- Retina is an outgrowth of diencephalon
- Mesencephalon (midbrain) is at junction b/w middle and posterior cranial fossa.
- Superior colliculus is present in upper midbrain and EWN of oculomotor nerve is situated here.
- Inferior colliculus is present in lower midbrain and trochlear nerve nucleus is situated here.
- Facial colliculus is present at level of pons

- Rhomboid fossa is a diamond shaped floor of 4th ventricle formed by medulla and pons.

- Basal plate of neural tube : gives rise to motor nuclei
- Alar plate of neural tube : gives sensory nuclei (somatic afferent column) + cerebral hemisphere & cerebellum
- Roof plate of neural tube : ependymal cells, choroid plexus of lateral, 3rd & 4th ventricle.
- Parvocellular pathway from LGB to visual cortex is most sensitive for the stimulus of colour contrast

Brain Stem

○ Gaze centres

- The gaze centres for horizontal movements of the eyes are located in **pons** near the abducent nucleus in PPRF (para-median pontine reticular formation).
- The gaze centres for vertical movements of the eyes are located in the **midbrain** in rostral interstitial nucleus of MLF, nucleus of Cajal, and neurons of tegmentum. Lesion produces paralysis of vertical (upward/downward) gaze. [Mnemonic HPVM]

- The MLF (medial longitudinal fasciculus) plays a role in co-ordination of vertical & horizontal conjugate movements of the eyes. U/L Lesions of MLF produce internuclear ophthalmoplegia.
- **Attention centre:** The **locus coeruleus**, which contains largest concentration of NA melanin containing neurons, functions as attention centre.

Cerebellum

- Cerebellum is connected to brain stem by three cerebellar peduncles (CPs).

Mid brain	---	by superior CP
Pons	---	by middle CP
Medulla	---	by inferior CP

○ Parts of cerebellum :

Part	Formed by	Function	Effect of lesion
Archio	Flocculonodular lobe + lingula	Projects to nu. fastigius	Swaying, positional nystagmus
Paleo	Anterior lobe Nu. emboliformis + nu. globosus	Controls posture, tone & crude movements	
Neo	Middle lobe	Fine movements	Past pointing, dysmetria, dyssynergia, hypotonia

○ Cerebellar cortex :

- Cerebellar cortex has 3 layers, which contain five cell types [Does not include bipolar cells]
 1. Outermost molecular layer : Stellate , Basket cells
 2. Middle layer --- **Purkinje cells**
 3. Inner (deeper/granular) layer : **Granule, Golgi cells.**
- Purkinje cells are the only output cells (efferent) from the cerebellum and they are always inhibitory (GABAergic). The remaining four cells are afferent in nature.
- Mossy fibres excite → Granule cells → excite the remaining four cells via the parallel fibres.

→ Climbing & Mossy fibres are excitatory in nature (these are 2 main inputs to the cerebellum)

→ Afferent cells which are the basket cells (located in molecular layer), Stellate cells (located in superficial layer) and Golgi cells (in granular layer) are example of inhibitory interneurons.

→ Bipolar cells are present in the cerebral (NOT cerebellar) cortex and retina.

→ In grey matter of CNS dendritic tree grows max^m in the postnatal life.

Neocortex

- Also called neopallium or isocortex.
- The neocortex is part of the cerebral cortex (along with the archicortex and paleocortex, which are cortical parts of the limbic system).
- Long term memory is stored in neocortex. In all mammals, it is involved in "higher functions" such as sensory perception, generation of motor commands, spatial reasoning, conscious thought and language.

Hippocampus

- The FORNIX is a band of nerve fibers that connects the hippocampus to the hypothalamus.
- The hippocampus is responsible for sending information to appropriate parts of the cerebrum for long-term memory.
- The mammillary bodies are a pair of small round lobes located at the end of the fornix.

Neostriatum

- The striatum, also k/as the neostriatum or striate nucleus, is a subcortical (i.e., inside, rather than on the outside) part of the forebrain.
- The neostriatum is the entryway into the basal ganglia and is the site of many of the neurological defects involving basal ganglia function.

- Cortical glutamatergic and nigral dopaminergic afferent input impinge on neurons in the neostriatum, providing the most significant afferent inputs to this structure.

WHITE MATTER OF CEREBRUM

• Association (Arcuate) fibres:

Cingulum, uncinate fasciculus, superior and inferior longitudinal fasciculus

• Projection fibres: CST, corticopontine tract and other tracts (Pyramidal tract)

• Commissural fibers : Corpus callosum

- *Hippocampus is connected to hypothalamus by fornix.*
- *The amygdala is an almond shaped structure involved in emotional responses, hormonal secretions and memory.*
- *Nerve supply of piriform cortex is ipsilateral olfactory nerve.*

Internal Capsule

Part	Fibres (descending)	Fibres (ascending)
Anterior limb	Frontopontine	Anterior thalamic radiation
Genu	Corticonuclear	Anterior part of superior thalamic radiation
Posterior limb	Cortico-pontine CST, CRT	Sup. thalamic radiation Fibres from lobus pallidus to subthalamic nucleus
Retrolentiform part	parieto-temporo-, occipito to pontine fibres	Post thalamic radiation
Sub-lentiform part	connections b/w temporal lobe and thalamus	Auditory radiation

THALAMUS

- All thalamic nuclei send axon to different part of cortex except reticular nuclei.
- Dorsal group of thalamic nucleus (**pulvinar** nu., intralaminar nu, rostral / anterior nucleus) project to neocortex.
- VPL group of thalamic nuclei carry pain & temperature sensation.

BLOOD SUPPLY OF BRAIN / CEREBRAL HEMISPHERE & EFFECT OF LESION

- Single limb paralysis (Monoplegia) is d/to injury to area 4.

Arteries of Brain & Effects of their lesion

Lesion of artery	Site of lesion	Result
Penetrating br. (Heubner's)	Ant. limb of IC, head of caudate nucleus	Ataxia, apraxia, tremors of opp. limbs,
ACA, cortical br.	Medial & superior surface of fronto-parietal cortex	Cont/L LL Paralysis, Rectal/urinary incontinence, Gait disturbances
PCA	1 ^o visual area	C/L Homonymous hemianopia
	Cerebral peduncle	Peduncular hemiplegia
	Medial temporal lobe	Amnesia
	Thalamus	Thalamic syndrome
Vertebro-basilar a.	Midbrain	Weber's Claude's (crossed cerebral lesions)
	Pons	Millard- Gubler
	Medulla	Palatal paralysis, Schmidt's syndrome
ASA br. of vertebral a.	Medial region of medulla	Medial medullary syndrome
	- Pyramid	c/L hemiplegia (UMN)
	- Hypoglossal nu.	ipsi/L tongue paralysis (LMN)
	- Medial lemniscus	c/L loss of conscious proprioception, touch, vibration
PICA br. of vertebral a.	Postero-lateral region of medulla	Lateral medullary syndrome (Wallenberg or PICA syndrome)
MCA, Cortical br.	Lat. surface of cerebral hemisphere	Sensory motor cortex (C/L hemiplegia +hcmianaesthesia), Motor & sensory speech centre (Broca's, Wernicke's), Optic radiation (homonymous hemianopia)
MCA, penetrating br.	Putamen, globus pallidus, Genu, post radiation of IC Spinal cord	Dense sensory motor hemiplegic syndrome

Hippocampus

- Sea horse shaped part of cerebral cortex which bulges in the floor of inferior horn of lateral ventricle.
- Also described as **ram's horn** or Ammon's horn.
- CA1 (Sommer's sector) neurons of hippocampus are most sensitive to hypoxia.
- Plays role in learning, recent memory, & control of emotional behaviour.

SPINE AND SPINAL CORD

- Subdural space ends at the level of — S_2
 - Dura mater & subarachnoid space ends at level of — Lower border of S_2
 - Spinal cord ends at level of
 - Lower border of L_1 or L_1-L_2 in adult
 - Lower border of L_3 or L_3-L_4 in children
 - S_4 (upto 3month of intrauterine fetal life).
 - Site of puncture in lumbar puncture ----- Below L_2 (preferably L_3-L_4 in adults & L_4-L_5 in children)
 - Piamater extends upto — Tip of coccyx
 - Largest vertebral body - in lumbar region.
- **Filum terminale & ligamentum denticulatum** — both are derived from pia mater
 → **Cisterns** (eg. cisterna magna / cisterna pontis) — are dilatation of subarachnoid space
 → **Critical vascular zone of spinal cord** is T_4-T_8
 → **Artery of Adam Kweicz** extends between T_9-T_{11}
 → **Central canal** is central in the lumbar region
 → **Disc** are NOT found b/w — C_1-C_2 and sacrum-coccyx
 → **Least permissible movement at lumbar spine** is — rotation

Spinal Cord level for Deep tendon Reflexes

Reflex/Jerk	Spinal level	Nerve affected
Biceps jerk	C5C6	Musculocutaneous
Triceps	C7 C8	Radial
Brachioradialis	C5C6	Radial
Patellar/ Knee Jerk	L3L4	Femoral
Ankle	S1S2	Tibial

→ **Supinator jerk** is mediated by $C_5 C_6$

→ **Inverse supinator** is mediated by $C_5 C_6$ Lesion

ORAL CAVITY

PALATINE/ FAUCIAL TONSIL

- Develops from ventral part of **2nd pharyngeal pouch**.
- N/s: Supplied by lesser palatine br. of maxillary nerve, IXth CN
- L/D : Jugulo-diaphragmatic nodes
- B/s: Tonsillar br. of facial a., ascending palatine a., greater palatine br. of maxillary a., ascending pharyngeal br. of ECA, dorsal br. of lingual a.
- Lining by non-keratinised stratified squamous epithelium.
- V/d : Paratonsillar vein.

Waldayer's Ring

- Ring of lymphatic aggregates in the nasopharynx & oropharynx.
- Composed of MALT tissues.
- Formed by
 - b/L faucial/palatine tonsils
 - b/L tubal tonsils
 - Nasopharyngeal tonsils(adenoids)
 - Lingual tonsils
- Provides local defense & produce T & B lymphocytes.

THYROID GLAND

- Plane of Cleavage in thyroidectomy** (compared to prostatectomy)

	In Thyroidectomy	In prostatectomy
Plane of cleavage	B/w false & true capsule	Beneath true capsule
Capsule which is left behind	False	Both
Ligation of artery	Superior TA is ligated near	

[Mnemonic to remember **RIA SEN**

RIA = to save **R**ecurrent laryngeal nerve **I**nferior thyroid artery is ligated **A**way.

SEN = **S**uperior thyroid a. is ligated to save **E**xternal laryngeal nerve **N**ear the gland.]

- Arterial supply of the gland is:
 - Superior TA. (branch of ECA)
 - Inferior TA. (branch of thyrocervical trunk)
 - Thyroidea ima (branch of brachiocephalic)

4. Lowest T.A. (Trunk/arch of aorta)
- Parathyroid gland is s/by inferior thyroid artery.
- Venous drainage of the gland is :
 1. Superior TV → Common facial v.
 2. Middle TV → IJV
 3. Inferior TV → Lt. brachiocephalic v.
 4. 4th T.V. of Kocher's → IJV

THYMUS

- Develops from endoderm of 3rd pharyngeal pouch
- Histologically there are 2 parts. Cortex and medulla
Cortex --- Lymphocytes (95% T-cells) are cortical.
Germinal centres appear in autoimmune d/s (normally absent)
Medulla --- **Hassall's corpuscle**, epithelial cells which secrete lymphopoietin (competence inducing factor) & form blood thymus barrier
- At birth its weight is 10-15 gm, weight increases 30-40 g at puberty and regresses after that. However thymus is believed to produce T-lymphocytes throughout life.
- Involution of thymus is
Enhanced by – hypertrophy of adrenal cortex, injection of cortisone / testosterone
Delayed by – castration/adrenalectomy
- B/S – branches from inferior thoracic and inferior thyroid artery.
- N/S – Vasomotor nerves derived from stellate ganglion. capsule is s/by phrenic nerve
- L/D – It does not receive any lymph vessels, but gives off efferent vessels.
 - *Stare cells, stellate cells and malpighian bodies are present in spleen*
 - *Kupffer cells are present in liver*
 - *Reticular cells, plasma cells, memory cells are present in LN.*

TONGUE N/S

Sensory

- Chorda tympani is the nerve of taste (except circumvallate papillae) and lingual nerve carry general sensaⁿ from anterior 2/3rd of tongue.
- Glossopharyngeal nerve is the nerve for both general sensation and taste from posterior 1/3rd of tongue including circumvallate papillae.
- Internal laryngeal branch of vagus nerve carry both

general sensation and taste from posterior most portion or vallecula

Extract:

Part of tongue	General sensation	Taste sensation
1. Ant 2/3 rd	Lingual n. (br. of mandibular V ³)	Chorda tympani br. of facial n.
2. Post 1/3rd, circumvallate	Glossopharyngeal nerve	Glossopharyngeal nerve
3. Posterior most, vellucela	ILN	ILN
4. Larynx, epiglottis, esophagus	ILN	ILN

[Mnemonic General 5,9,10/ Taste 7,9,10/ motor 12,11]

- *Afferents from palate travel via GSPN to geniculate ganglion and thence via the facial nerve to brainstem*
- *ILN (Internal laryngeal nerve) is a branch of superior LN which is a br of vagus*

Motor

All muscles of tongue are s/by hypoglossal nerve except palatoglossus which is s/by cranial accessory nerve through pharyngeal plexus

Types of Taste Buds

- **Foliate papillae** --- Located along the lateral margin of tongue.
- **Fungiform papillae** --- Located throughout the dorsum of tongue.
- **Circumvallate papillae** --- At junction of dorsum and base of tongue.

Taste buds are also located in the palate, epiglottis, larynx and esophagus.

ESOPHAGUS

- Length of esophagus is 25 cm or 40cm from the incisor teeth.
- Extends frm lower border of cricoid cartilage C₆ to T₁₁.
- Pierces the diaphragm @ T₁₀.
- 4 constrictions : (CALD)
 - 1) Cricopharyngeal region @ C₆, 15cm frm incisor
 - 2) Aortic @ T₄, 25cm
 - 3) Left bronchus @ T₆, 27 cm
 - 4) Diaphragm @ T₁₀, 40 cm
- **Histo** : Serosa is absent. Muscularis externa is the toughest layer. (In small bowel submucosa is strongest). Only auerbach's plexus is there.

- Epithelium is stratified sq non-keratinised. Distal 1-2 cm its junctional columnar.
- *B/s of esophagus:-*
 1. Cervical part - Inferior thyroid artery
 2. Thoracic part - Bronchial artery
 3. Abdominal part - Lt gastric & inferior phrenic artery.
- UES - high pressure zone, 3-4 cm long, relaxes during swallowing
- LES : high pressure zone, 3-5 cm, pressure is 30 cm H₂O.
- Esophageal peristaltic pressure : 25 - 80 mmHg.
- Negus type esophagoscope is with proximal illumination, rest all are distal.
- Classical bougie for dilatation is Chevalier Jackson.
- Gold standard for GERD is 24hr pH measurement.
- Endoscopy is C/I in Zenker's diverticulum
- Corrosive strictures of esophagus are d/to - NaOH / lye
- *Perforation:* M/c cause of esophageal perforation is iatrogenic. M/c site of perforation is CRICOPHARYNX
- *Diverticula:*
 - Pulsion* diverticula are caused by high pressures - proximal to UES & LES. E.g. Zenker's
 - Midesophageal diverticulum is a *traction* diverticulum
- Esophagitis changes are max^m in the LEE (Lower esophagus end)
- *Esophageal atresia* : M/c type is type I ...proximal segt ends blindly & distal end communicates with trachea. The sign of TEF is continuous pouring of saliva. In TEF contrast X-ray is taken in supine position. Rx of TEF is rt sided thoracotomy. Most dreaded post op complication of TEF is pneumonia from anastomosis.
- *Esophageal strictures:* Endoscopy is done within 24hrs if possible. Radiographs are done on 10-14 days to determine the development of strictures. Dilatation 3-4 wks after ingestion.
- BOERHAAVE'S syndrome - vomiting with a full stomach, longitudinal tear in the lower esophagus
- MALLORY WEISS TEAR - d/t repeated vomiting massive upper GIT bleeding, **partial thickness tear** in the LEE usually below the esophagogastric jn, So Sengstaken tube is not advised.
- Upper esophageal webs → PLUMMER VINSON SYNDROME
- Lower esophageal webs → SCHATZKI RING'S in those with reflux esophagitis.
- Diffuse esophageal spasm - CORK SCREW or ROSARY ESOPHAGUS
- DYSPHAGIA LUSORIA → constriction by aberrant right subclavian A., vas rings or double aortic arch.
- BARRET'S ESOPHAGUS - Presence of columnar epithelium 3cm above EG junction, pre-malignant condition. Predisposes Ca-esophagus.
- M/c esophageal hernia is SLIDING HERNIA: EG junction is at a higher level, no typical hernial sac, a/w GE reflux.
- ROLING HERNIA is the true esophageal hernia ----- EG jn @ N level, typical hernial sac is present, not a/w GE reflux
- Achalasia cardia is loss of ganglion cells in the Auerbach's plexus. **Rat tailed deformity**, S-shaped bend, lack of gas bubble in stomach, mecholy test +ve, 10 fold ↑ in carcinoma. Heller's cardiomyotomy is done
- M/c benign neoplasm of esophagus → Leiomyoma.
- M/c malignancy of esophagus - SqCC. M/c site is middle 1/3rd.
- *Pre-malignant lesions :*
 - Plummer vinson syndrome
 - Achlasia
 - Hiatus hernia
 - Reflux esophagitis
 - Barrett's esophagus
 - Irradiation, corrosive esophagitis
 - Esophageal diverticulum
- Anti-reflux surgeries for GER
 - Nissen's fundoplication
 - Besley Mark IV
 - Hill's posterior gastropexy
 - Leigh collis gastropasty
 - Angelchik prosthesis
- *Rx of Ca. esophagus :*
 1. Post cricoid - RT / Pharyngolaryngectomy

2. Upper third - RT / Mc Keown's 3 stage esophagectomy
3. Middle third - RT / Ivor Lewis
4. Lower third - esophagogastricomy with Roux en Y.

[No RT because most of the lesions are adenocarcinoma]

Palliative :

Tubes gastrostomy, Chemo with 5 - FU.

LUNGS/THORAX

- Lung differentiation occurs in pseudoglandular stage.
- Structures arching over hilum of right lung --- Azygos vein.
- Structures arching over hilum of left lung --- Arch of aorta.

Bronchopulmonary Segments (BPS)

- Part of lung tissue aerated by a tertiary bronchi is k/as BPS.
- BPS is an anatomical, functional and surgical unit of lung.
- Both lungs have 10 BPS (sometimes 8 -9 on the Lt. side).
- Rt middle lobe have 2 BPS - Medial & lateral.
- BPS does NOT have its own vein. Pulmonary vein is intersegmental & it drains BPS.
- Apical (superior) segment of lower lobe is related to posterior parts of 4-8 ribs and c/b examined in the "triangle of auscultation".
- Medial basal (cardiac) segment is inaccessible for physical examination through chest wall.
- Lingular segment is present on left side in Left Upper Lobe (= LingULa)
- BPS most commonly involved in ---

BPS	Lobe	Involved in
1. Apical (superior) segment	RLL	Aspiration in supine/comatose, aspiration pneumonia, atelectasis
2. Anterior segment	RUL	Lesions tend to be cancerous
3. Apex	RUL	Pancoast tumour
4. Posterior segment	RUL	TB, Septic pneumonitis, aspiration abscess
5. Posterior segment	LLL	Bronchopulmonary sequestration
6. Basal segments	LL (Lt > Rt)	Asbestosis, Bronchiectasis

- Mendelson syndrome is the aspiration pneumonitis in Apical (superior) segment of Rt lower lobe (RLL). In the supine position the superior segmental bronchus is most dependent part of lung.
- Intralobes are some extra lobe type b/n lower lobe and diaphragm.
- Lung abscess ---- M/c site is lower part of RUL or upper part of the RLL
- Bronchiectasis ---- Left lower lobes (or B/L lower lobes)
- TB, Silicosis involve upper lobes of lungs

→ Right principal bronchus is wider, shorter and more vertical, so prone to FB lodgement

→ For pneumonectomy the approach is usually a posterolateral thoracotomy through the bed of 6th rib.

→ M/c site of bronchogenic cyst is in relation to carina.

Fissures:

The oblique fissure divide the lung on both sides into upper and lower lobes. The fissure extends on the left from the tip of the spinous process of the T2-T3 vertebra to the level of 6th costochondral junction anteriorly.

The horizontal fissure of the lung is a recess in the parenchyma of the right superior lobe. Right middle lobe lies below the fissure

Lung vessels:

Bronchial arteries

Supply the non-respiratory (conducting) part i.e. upto terminal/ respiratory bronchioles. They may contribute to venous admixture b/w systemic and pulmonary circulation and have nutritive function.

Pulmonary arteries

Pulmonary arteries are involved in gas exchange. They supply respiratory part (alveoli).

Pulmonary Hypoplasia

- Most commonly a/w Bochdalek's congenital diaphragmatic hernia. May be a/w oligohydramnios and eventration of diaphragm

Parietal pleura/Costodiaphragmatic recesses

- Costodiaphragmatic recesses are the largest and clinically most important.
- Inferior border of parietal pleura (or costo-diaphragmatic line of pleural reflection) ends at

- Ends in mid clavicular line --- at level of 8th rib.
- Mid axillary line --- at level of 10th rib.
- In posterior axillary line --- at 12th rib level (which correspond to upper part of body of T₁₂)

Lower margin of lung is 2 ribs higher than the l/o parietal pleura

- During quiet respiration, the inferior margin of lungs crosses rib 6 in the midclavicular line, rib 8 in midaxillary line and then courses to vertebral level T10.
- Costodiaphragmatic pleural recess are most dependent part of pleural cavity where fluid can easily accumulate. It is also the largest of pleural recesses.

Ribs

- Shortest, broadest & most curved : 1st rib
- Typical ribs : 3-9
- True ribs/vertebrosternal ribs (cartilage connected to sternum) : 1-7
- Typical IC nerve : 4-6
- Costal margin formed by : 7-10
- Typical vertebrae : 2-8
- False ribs/vertebrochondral : 8-12
- Floating ribs (vertebral ribs) : 11, 12

TRACHEA

- Extend from lower border of cricoid cartilage (opposite C6 vertebra).
- Length 11 cm.
- It bifurcates at lower border of T4 (carinal level) which may be lower upto T6 in standing
- First 16 generations are conducting zone i.e. trachea, bronchi, bronchiole, and terminal bronchioles
- Last 7 generations i.e. respiratory bronchiole, alveolar duct, alveoli and alveolar sac are respiratory vessels
- B/s is by inferior thyroid artery
- Thyroid swelling are the m/c cause of compression of trachea.

DIAPHRAGM

- Diaphragm is mesodermal in origin. It develops from fusion of septum transversum (central tendon), dorsal esophageal mesentery, pleuroperitoneal membranes and body walls.

- M/s of diaphragm develops from 3,4,5 cervical myotomes and hence its motor innervation is from phrenic nerve which arises from ventral rami of C₃ C₄ C₅. It is also sensory to central part. Sensory supply of the lateral part of diaphragm (muscles) is by intercostal nerves.

Diaphragmatic openings:

Level -	T8	T10	T12
Openings	IVC (Venacaval opening)	Oesophagus (Oesophageal hiatus)	Aorta (Aortic hiatus)
Content	Rt. phrenic n.	Vagus nerves (Rt. & Lt.)	Thoracic duct - lies Rt. to aorta
		Lt. Gastric artery	Azygos vein
Part of diaphragm	(in central tendon)	(in muscular part)	(in osseaponeurotic opening)

[Mnemonic to remember from above downwards – VOA Voice Of America (for Vena caval, Oesophageal, Aortic openings respectively at 8, 10 and 12 thoracic levels.)]

- The left phrenic nerve passes through muscular portion of diaphragm not through vena caval opening.
- Level of Diaphragm is : highest in - Supine, intermediate in - standing & lowest in - sitting position.
- Eventration of diaphragm : Congenital defect in musculature of left half of diaphragm in which diaphragm is pushed upward.

Congenital Diaphragmatic Hernia

	Retrosternal (Morgagnian)	Posterolateral (Bochdalek)
1. Frequency	Rare	M/c type of congenital DH
2. Occurs through	Foramen of Morgagni/ Space of Larry	Foramen of Bochdalek/ vertebro - costal triangle /pleuroperitoneal space
3. A/w	Herniation of transverse colon	Pulmonary hypoplasia
4. Location	Usually on Rt side, anteriorly	Usually on Lt side, posteriorly
5. Cl/f	Asymptomatic, M/c viscous involved is transverse colon	Triad of respiratory distress + dextrocardia + scaphoid abdomen

Acquired/Hiatus Diaphragmatic Hernia

	Sliding type	Rolling type
1. Frequency	85%	Less common
2. Occurs through	Esophageal opening	Esophageal opening
3. A/w	Short esophagus	-
4. Cardio-esophageal junction	Passes through	Intact
5. Cl/f	Reflux	No reflux

- M/c type of DH - Hiatus hernia
- M/c type of congenital DH (CDH) is - Posterolateral hernia of Bochdalek.
- Hiatus hernia is usually acquired. It occurs through esophageal hiatus in posterior mediastinum. Rolling type may be congenital d/to persistent peritoneal process in posterior mediastinum.
- Traumatic hernia is usually seen in bullet injuries

HEART

Development

- Heart is the first organ to start functioning in human embryo.

Truncus arteriosus gives rise to --- ascending aorta, pulmonary trunk. Spiral septum is in between.

Development of the IVS:

1. The muscular part develops from the floor of bulboventricular cavity.
 2. Membranous part develops from bulbar ridge, and endocardial cushion proliferation.
- Tetralogy of Fallot (TOF) is a relatively common anomaly, accounting for about 8% of congenital heart defects. The embryological defect is believed to be unequal division of the truncus arteriosus and conus cordis by the aortopulmonary septum.
 - **Fossa ovalis:**
 1. Primary septum of fetal heart.
 2. A saucer shaped depression in lower part of interatrial septum.
 3. Failure of fusion of 2 septa (1° & 2°) gives persistent foramen ovale.
 - The *septomarginal trabeculae* (*moderator bands*) are seen in rt ventricular apex.

Structures contained in/Related to

	Rt	Left
○ Atria	Torus aorticus, Koch's triangle	McCallum's Patch (Posterior wall)
○ Ventricles	Moderator bands (septomarginal trabeculae),	

Structures forming

Anterior surface of heart (sternocostal surface)	<ul style="list-style-type: none"> ○ RV mainly ○ Partly by LV and left auricle
Right heart border	<ul style="list-style-type: none"> ○ SVC ○ RA ○ IVC
Left heart border	<ul style="list-style-type: none"> ○ LV mainly ○ Aortic knuckle ○ Pulmonary artery ○ Left atrial appendage
Inferior border/ surface (diaphragmatic surface)	<ul style="list-style-type: none"> ○ RV + some part of LV
Base (posterior surface)	<ul style="list-style-type: none"> ○ LA receiving 4 pulm. veins, some part of RA
Apex	<ul style="list-style-type: none"> ○ LV

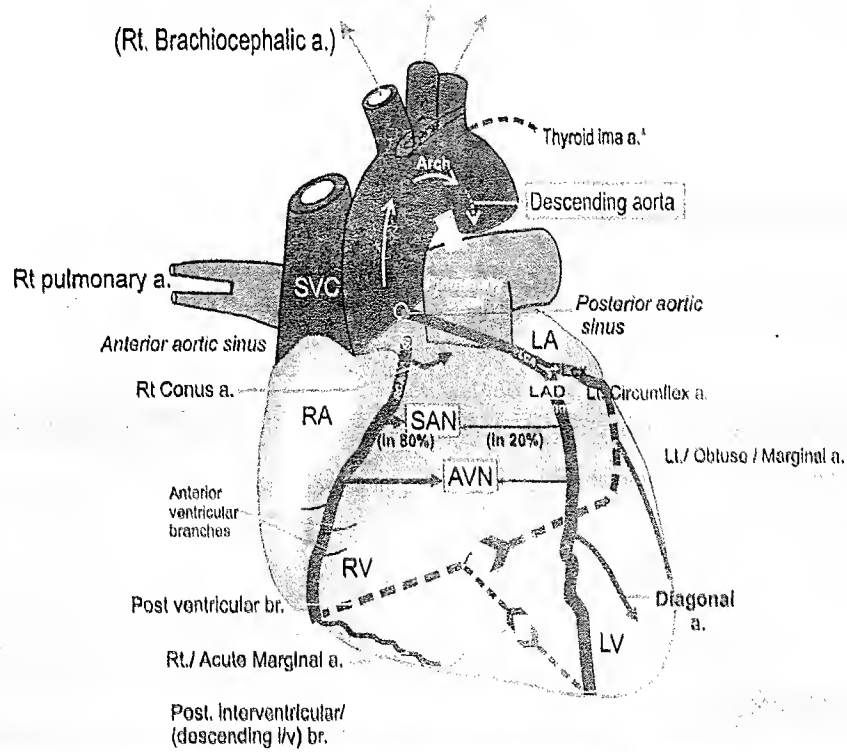
→ LA forms post-surface (base) of heart and lies behind RA. Posterior surface of LA forms anterior wall of oblique sinus of pericardium which separates LA from esophagus posteriorly. LA does not extend to the diaphragmatic surface.

→ Membranous part of atrioventricular part of IVS lies b/w RA and LV.

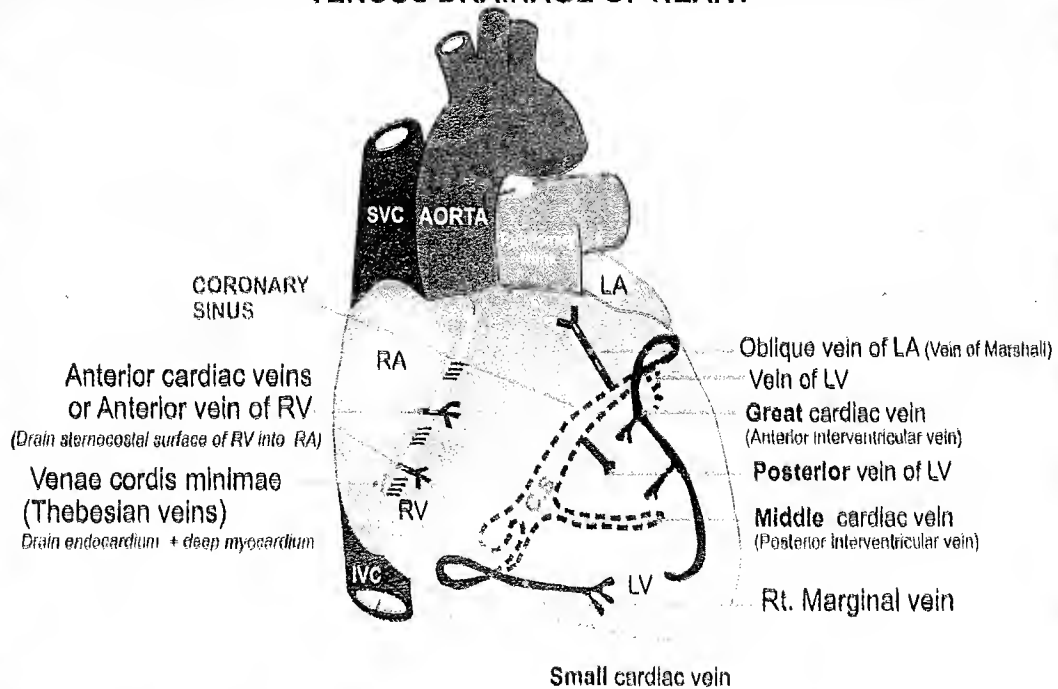
Lymphatics drain into tracheobronchial + mediastinal LN.

- Sympathetic innervation is by T₂ - T₆. The pain of pericarditis originates in the parietal layer (parietal pericardium) only, and is transmitted by the **phrenic nerve**.
- Rough portion of RA interior form a series of horizontal ridges like the teeth of a comb (**pectinate muscles**)
- Orifice of coronary sinus is guarded by **Thebesian valve** while IVC orifice is guarded by rudimentary eustachian valve (SVC orifice has no valve).
- The *torus aorticus* is the **bulge in the right atrial wall** above the atrioventricular membranous septum, produced becoz medial portion of the free wall lies against the right aortic sinus (aortic bulge).

BLOOD SUPPLY OF HEART



VENOUS DRAINAGE OF HEART



- The *coronary sulcus* is a horizontal groove b/w atrium and ventricles named so because it lodges the coronary vessels including coronary sinus.
- **Atrioventricular groove (sulcus)** lodges RCA
- **The anterior interventricular groove (or sulcus)** lodges the anterior interventricular artery (= LAD), a br. of LCA & the great cardiac vein.
- **The deep cardiac plexus** is located in front of the bifurcation of trachea.
- The *Koch's triangle* is an important landmark in the RA. It is bounded by- Valve of coronary sinus (posteriorly), tendon of Todaro (superiorly) & the attached margin of the septal cusp of tricuspid valve (anteriorly).

Tributaries of coronary sinus

- Drain into post wall of Rt. atrium
 - Great, middle & small cardiac v.
 - Post. vein of LV (left posterior ventricular vein)
 - Oblique vein of LA (Marshall)
 - Rt. marginal vein

Veins directly draining into RA

- **Anterior cardiac vein + venae cordis minimi**
(Thebesian / smallest cardiac v.)

B/s of Heart : Coronary arteries -

	RCA	LCA
1. Distribution	Smaller	Larger branch
2. Arises from	Ant. aortic sinus	Left post. aortic sinus
3. Lodged in	Anterior IV groove	Posterior IV groove
4. Supplies	- RA - Small part of LV near post IV groove. - Posterior part of IV septum. - Conducting system of heart except a part of left branch of AV bundle.	- LA - Greater part of LV - Ant. part of IV groove. - Part of left branch of AV bundle.

M/c arteries involved in MI's

Type of MI	M/c artery involved/blocked
1. Ant. wall MI	LAD
2. Inferior wall MI	RCA (Posterior interventricular or posterior descending branch)
3. Anteroseptal MI	RCA
4. Lateral wall MI	LCx

- Anterior 2/3rd of interventricular septum is supplied by ascending branch of LAD artery. While posterior part of IVS is supplied by RCA.
- LAD is a branch of LCA & is mostly affected by atherosclerosis. Also k/as anterior interventricular artery (widow's artery).
- Kugel's artery, diagonal artery and obtuse marginal artery are branches of LCA.
- Posterior descending artery and marginal artery are branches of RCA.

SA node (SAN)

- Located at the junction of SVC with RA **subepicardially** & superolaterally.
- Conduction system is made up of specialized (modified) nodal cardiac muscle. includes SA node, AV node, bundle of His and Purkinje fibres.
- *SA node is normal 'cardiac pacemaker' its rate of discharge determines the rate at which heart beats.*
- SAN is supplied by RCA in 60% of cases (and LCA in 40% of cases).

- *AV node is located in the Rt posterior portion of Rt atrium. For AV node Koch's triangle is an important landmark.*
- *SA node discharges most rapidly.*
- *Conduction velocity (rate) is highest in Purkinje system. It is 4 m/s.*

AORTA

- Arch of aorta starts at T4 level, reaches T3 and ends at T4. Corresponds to costal cartilages 2nd and 3rd.
- Aortic arch develops from - aortic sac, its left horn, left 4th artery, left dorsal aorta.
- Aortic arch is located in superior mediastinum.
- Branches of aortic arch:
 - Rt. brachiocephalic (further divides in Rt CCA, Rt s/c)
 - Common carotid
 - Lt subclavian
- **Tracheal tug** is a clinical sign of aneurysm of aorta.

UPPER LIMB

Erb's paralysis

- Injury to Erb's point (C5 + C6) i.e. upper trunk of brachial plexus leads to Erb's paralysis.
- *Nerves affected* : Musculocutaneous, axillary, nerve to subclavius, suprascapular

- *M/s involved* - biceps, brachialis, brachioradialis, deltoid mainly & partly-supraspinatus, infraspinatus, supinator
- *Deformity* - Policeman's tip hand / Porter's tip hand (Arm is adducted and medially rotated)

Klumpke's Paralysis

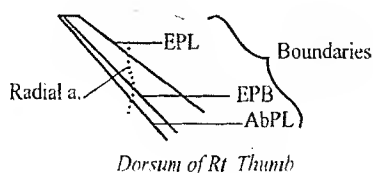
- Lower trunk of brachial plexus involved ($T_1 + C_8$)
- *Cause* : Undue abduction of the arms.
- *Deformity* : Claw hand.
- *Effect* : Horner's syndrome, Vasomotor, trophic changes, cutaneous anaesthesia of the ulnar border of arm & forearm.

Palmar Arches

- *Superficial palmar arch* is an anastomosis fed mainly by the ulnar artery. 1/3rd of the arch is formed by the ulnar artery, 1/3rd by the superficial palmar branch of the radial artery & 1/3rd by the arteria radialis indicis or the median artery. It lies at the level of distal border of extended thumb.
- *Deep palmar arch* is mainly formed by the terminal part of radial artery.

Anatomical Snuff Box

- Lies b/n following boundaries
EPL (Medial/posterior wall)
EPB+AbPL (Lateral/anterior wall) on radial side
- Scaphoid bone c/b palpated in box. Scaphoid # causes tenderness in snuffbox.
- Pulsation of radial artery are palpated here.
- *Contents*
1. Radial artery
2. Superficial/cutaneous branches of radial nerve
3. Cephalic vein (begins in snuffbox from radial side of dorsal venous network)
- *Floor is f/b/y*
1. Styloid process of radius (proximal)
2. Base of 1st MC (distal)
3. Scaphoid & trapezium (more deep)



Flexor retinaculum

- Structures passing superficial to FR are :
Median nerve & its cutaneous branches
Ulnar n. & vessels
Palmaris longus tendon

- Structures passing deep to FR are :
Carpal tunnel & its content + FCR

- Structures passing below or beneath flexor retinaculum are
1. Tendons of FDP, FDS, FPL and median nerve through carpal tunnel
2. Tendon of FCR
- Ulnar nerve and artery passes through cubital tunnel behind the elbow
- Deep terminal br. of ulnar nerve passes through Guyon's canal (Pisohammarate tunnel) under cover of pisohammarate ligament
- Ulnar nerve enters the palm passing superficial to flexor retinaculum (transverse carpal ligament) lying just lateral to pisiform. Here ulnar n. & artery lie under cover of a fascial band k/as volar carpal ligament, the space under it is k/as ULNAR TUNNEL.
- Structure passing through tarsal tunnel is posterior tibial nerve

Infections of Palm & their spreads

- Synovial sheath of FPL is k/as → Radial bursa.
- Synovial sheath of flexors of index, middle & ring fingers is k/as → Common flexor synovial sheath.
- Synovial sheath of FS & FP tendon is k/as → Ulnar bursa.
- Tenosynovitis of thumb can infect → radial bursa & that of little finger can infect the ulnar bursa → forearm space of **Parona** (resulting in hourglass swelling).
- Thumb & index finger spreads to → **thenar** space
- Middle, ring finger spreads to → **mid palmar** space
- Little finger spreads to forearm space of **Parona**, which is in continuity with the palmar spaces behind the flexor retinaculum through carpal tunnel.

- In 50% cases radial & ulnar bursa communicates with each other.
- Whitlow or felon is the infection of pulp space of finger.

GIT & ABDOMEN

STOMACH

- Average capacity : 1000-1500 mL. Capacity in a newborn is 30-50 mL.
- Blood supply : Via coeliac trunk.
- Cardia is 40 cm from incisor teeth.
- True pyloric sphincter is composed of thick circular m/s layer.
- Incisura angularis is a notch & is most dependent part in lesser curvature.

LIVER

- **Anatomical (Surgical) lobes** are divided into a large right lobe and small left lobe by line of attachment of *falciform* ligament anteriorly and fissures for ligamentum teres and ligamentum venosum inferiorly.

Lt lobe contains : Seg 2&3

Rt. lobe contains: Seg IV,V,VI,VII,VIII

- Physiological lobes are equally divided into right and Lt lobes by an imaginary line running from GB fossa to the centre of caudate lobe.
- **Cauinaud's classification** (French system) is based on V/D of liver i.e. hepatic veins (Rt,middle & Lt) and portal pedicles. Liver is divided into 8 segments.
 - Segment 1 contains Caudate lobe, which is drained by both Rt. & Lt. hepatic vein.
 - Segment 4 is quadrate lobe.
- American system divides the liver into 4 segments based on the relationship b/w hepatic & portal vein branches.

→ *Quadrate lobe (b/w lig. teres & fossa for GB) & caudate lobe are part of anatomical right lobe.*

But remember quadrate lobe belongs to physiological Lt lobe and caudate lobe is functionally part of both right and Lt lobe.

→ *Reidel's lobe is a tongue shaped downward projection from right lobe.*

- Inferior border of liver corresponds to transpyloric plane in midline
- Liver is covered by Glisson's capsule
- Cord of Billroth's are seen
- **Space of Disse** are perisinusoidal space in liver and contain cells of Ito (role in Vit. A synthesis) and Kupffer cells (liver macrophages)
- Arrangement of structures anterior to posterior at porta hepatis: DAV (Bile duct → hepatic artery → portal vein)
- Portal acinus is divided into 3 zones.
 - Zone 1 (Periportal) – more susceptible to toxic damage
 - Zone 2 (Mid zone)
 - Zone 3 (Central zone) - more susceptible to hypoxia
- Needle biopsy of liver is done by inserting needle in right 8th or 9th intercostal space.

PORTAL VENOUS SYSTEM

- **Valveless** system like vena cavae
- Portal vein is formed by SMV + splenic vein
- Normal portal pressure is 10 mm Hg. In portal hypertension it is 30-40 mm Hg
- Sites of portocaval anastomosis & their cl/f are:

- Lower end of esophagus (esophageal varices and hematemesis)
- Anterior abd. wall, periumbilical (caput medusae)
- Posterior abd. wall (internal hemorrhoids)
- Bare area of liver
- Intrahepatic
- Upper part of anal canal (internal hemorrhoids)

Obstruction of SVC, IVC, Portal vein

- *Portal venous obstruction :*

Flow is **away from umbilicus**. Centrally placed enlarged veins form cluster around umbilicus (caput medusae)

- *In SVC obstruction*

Blood flow is from **above downwards** because flow from intercostal vein (which normally drains into SVC) is diverted to IVC through inf. epigastric v.

- *IVC obstruction :*

Paraumbilical dilatation. Flow of blood is from **below upward**. Anastomotic channels opens (dilates/exaggerated) b/w superior epigastric vein and circumflex iliac vein.

- In splenic vein thrombosis large **gastric varices** (dilated gastric veins) are seen but esophageal varices are uncommon.

GALL BLADDER

- **Fundus** lies behind the tip of 9th costal cartilage.
- Neck is continuous with cystic duct. Cystic duct contains 5-12 spiral valve of Heister
- Hartman's pouch is a small projection from right side of the neck
- GB mucosa is lined by simple columnar epithelium with brush border cells
- **Murphy's sign** is tenderness elicited at Murphy's point in acute cholecystitis

PANCREAS

- Head of pancreas is retroperitoneal.
- 1st part of duodenum, transverse colon, Rt. lateral border of jejunum, SM vessels form anterior relations of pancreas.
- *Pancreatic ducts :*
There are two major pancreatic ducts --- Wirsung & Hoffmann's duct. They begin in tail but joins the bile duct in head of pancreas and forms ampulla of Vater, which opens on summit of major duodenal papilla (8-10 cm distal to duodenum).

- Accessory pancreatic ducts are Santorini & Bernard. They open into duodenum at minor duodenal papilla
- **Sphincter of Oddi** has 3 sphincters.
- Ectopic pancreatic tissues are most commonly seen in stomach.

Mesentery

- Fan shaped fold of peritoneum that attaches the jejunum & ileum to the posterior abdominal wall.
- Root of mesentery crosses : ascending & horizontal parts of duodenum (3rd/4th), abdominal aorta, IVC, right ureter/psoas/gonadal vessels.
- Directed obliquely downward and to the right.

APPENDIX

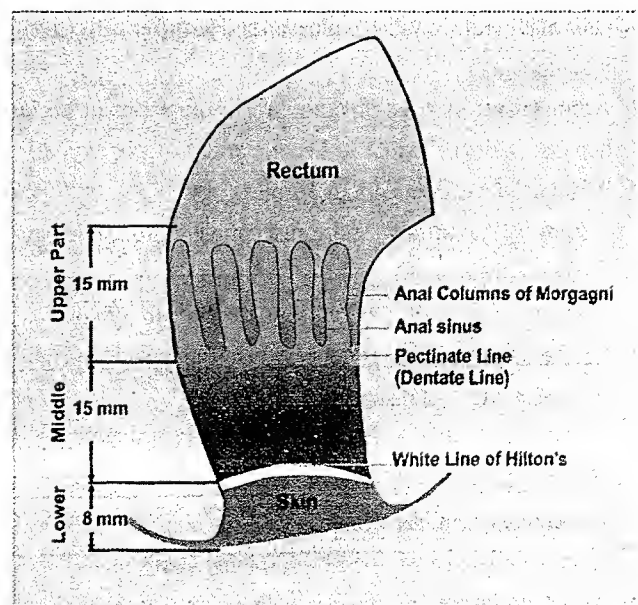
- M/c position is retrocecal (75%). Next common is pelvic 21% (Peri-ileal is rarest)
- *Appendicular artery* is a branch of ileocolic a. *Accessory appendicular a.* is a br. of ileocecal a. or inf. division of ileocolic a.
- Opening of appendix, into caecum is guarded by 'valve of Gerlach'.
- Submucosa contains numerous lymphatic aggregates / follicles k/as **abdominal tonsils**.
- Closely related to right lateral paracolic gutter. Appendix is a content of retrocecal recess.
- Referred pain is felt in the T₁₀ dermatome (periumbilical)
- **McBurney's point** is the site of max^m tenderness in appendicitis.
- *Gridiron incision* is an oblique incision placed at McBurney's point. It is used for conventional appendicectomy.

ANAL CANAL

- Anal canal is ~4 cm long. It extends from anorectal junction to the anal orifice.
- The muscular junction b/w the rectum and the anal canal is anorectal ring which can be felt as a thickened ridge on PR examination.
- Anal canal is divided into 3 parts:
 - i) Upper 15 mm : Contain 6-10 longitudinal folds of mucosa k/as **columns of Morgagni**.
 - ii) Middle 15 mm : Pecten
 - iii) Lower 8-10 mm: Lined by true skin. Sweat and sebaceous glands are also present.
- *Pectinate (Dentate) line* is the midpoint of anal canal, formed by anal valves or circumferential musculature of canal. It is a true muco-cutaneous junction located 1-1.5

cm above the anal verge. A 6-12 mm transitional zone exists above the dentate line over which squamous epithelium of anoderm becomes cuboidal and then columnar epithelium. The anatomic anal canal starts at the dentate line.

- *Anorectal ring* is formed by fusion of puborectalis, fibres of deep part of external sphincter and internal sphincter.
- *Valves of Houston* are 3 distinct folds of rectum.
- *Columns of Morgagni* are 6-10 longitudinal folds of mucosa found in upper third (upper 15 mm) of anal canal.
- *Anal valves of Ball* are transversely placed semilunar folds.
- *Pectinate line* is a transverse line, which divides b/w the endodermally derived and ectodermally derived anal canal. Thus it is also k/as watershed line. It runs all around the anal canal along the lower limit of the anal valves.
- *White line of Hilton* denotes the lower limit of pecten. Also called anal verge or anal margin.
- *External hemorrhoids* are very painful because they are below pectinate line and this region of anal canal is supplied by inferior rectal nerve which is a branch of pudendal nv.
- *External anal sphincter* is voluntary and is contributed by puborectalis fibres of levator ani. S/b S4 (inferior rectal nerve)



○ **Pectinate line separates:**

	Above	Below
1. Development	Endodermal	Ectodermal
2. Nerve/s	Autonomic nerves, thru inf. hypogastric plexus	Inf. rectal n. (somatic)
3. L/d	Internal iliac LN	Superficial inguinal LN (medial group)
4. B/s	Superior and middle rectal arteries	Inferior rectal a. (a branch of internal pudendal artery)
5. V/d	SRV (portal)	IRV (systemic)

- The caecum, appendix, ascending colon, and right 2/3rd of transverse colon (midgut derivatives) have sympathetic supply from coeliac and superior mesenteric ganglia, and parasympathetic supply from vagus.

- **Pelvic splanchnic nerves** carry sympathetic fibres to rectum and parasympathetic fibres via nervi erigentes (S2-S4) to hindgut derivatives e.g. rectum, bladder and uterus.

Structures palpable on PR examination

Post surface of UB, Seminal vesicles vas def.; prostate and its fascia, perineal body, UGD, bulb of penis.

UMBILICUS

- **Weeping umbilicus** is a term used for developmental malformation of allantois & VID.

a. **Persistent allantois/urachus** --- leads to urinary fistula at umbilicus.

b. **Persistent of VID** --- fecal fistula at umbilicus.

○ **Umbilical adenoma**

Is k/as *Raspberry tumour* but it is not a true tumour. It is formed from unobliterated VID

○ **Umbilical Granuloma**

Small flesh like pale nodule at the base of umbilicus with persistent discharge in newborn.

○ **Sister Joseph's nodule**

Secondary carcinoma at umbilicus. Seen in metastatic gastric adeno carcinoma.

INGUINAL REGION

- **Inguinal ligament:** Extends from ASIS to pubic tubercle.
- **Inguinal canal:** Situated just above medial half of inguinal ligament. 4 cm in length. Extends from DIR to SIR.

○ **Midinguinal point:**

A point midway between ASIS and pubic symphysis situated 1/2" below DIR. Femoral a. begins at this point

○ **Deep inguinal ring (DIR):**

- Oval opening of fascia transversalis situated 1/2" above and lateral to the mid inguinal point. It lies just lateral to inferior epigastric artery
- Transmits **spermatic cord in males & round ligament of uterus in females.**

○ **Superficial (external) inguinal ring (SIR):**

- Triangular gap in EO-aponeurosis, lies medial to inf epigastric artery just above pubic tubercle
- Transmit all contents of DIR + Ilioinguinal nv.

→ *Lacunar ligament forms medial boundary of femoral canal*

→ *Inferior epigastric artery is an important landmark at lateral border of Hasselbach's Δ which explains direct and indirect inguinal hernias.*

→ *Femoral ring is the medial most compartment of femoral canal (femoral sheath)*

→ *Conjoint tendon is f/by fusion of IO + TA. Sometimes it is continuous with a band / interfoveolar ligament.*

○ **Cremasteric reflex**

- Afferent: - femoral br. of genitofemoral (medial thigh)
- Efferent: - Genital br. of Genitofemoral n. (L₁). which is motor to cremaster muscle

→ *Cremasteric reflex is lost in testicular torsion*

→ *N/s of pyramidalis muscle is --- subcostal nv.*

→ *Cremaster n/s is s/by --- Genital br of genitofemoral nerve*

Spermatic cord transmits

Vas deferens + testicular & cremasteric a. + pampiniform plexus + genital branch of genito femoral nerve + remains of processus vaginalis (but does not transmit ilio-inguinal nerve).

Inguinal canal transmits

- Spermatic cord in males [or round ligament of uterus in female]
- Ilioinguinal nerve in both males and females.

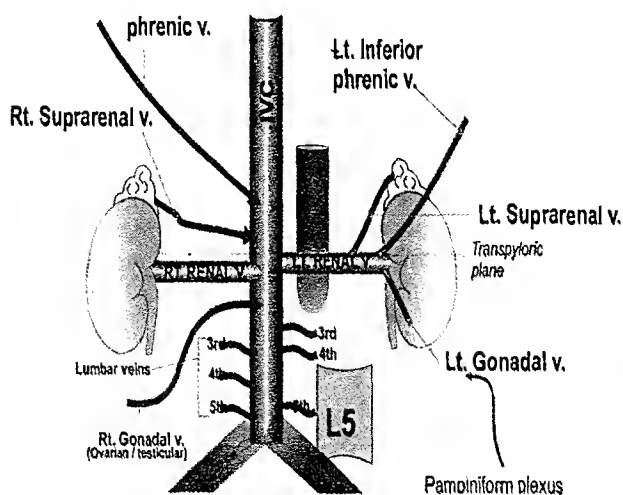
KUB REGION

KIDNEY

- Extent - T_{12} to L_3
- Right kidney is slightly lower because it is below liver. Left kidney is little longer and narrower
- Each renal artery divides into 5 segmental arteries. *Segmental arteries are end arteries.*
- M/c anomaly of renal vessels --- Accessory (supernumery) renal arteries in 30%.
- Lt. renal vein may double sometimes k/as persistence of renal collar
- Several stellate veins drain the most superficial zone of renal cortex.
- Left kidney is usually chosen for renal transplantation because it has longer renal vein. Transplanted kidney is placed in right iliac fossa, in the retroperitoneal region, leaving native kidney in situ.

VENOUS DRAINAGE

Lt renal vein receives left gonadal, left adrenal (suprarenal) and left inferior phrenic vein & then finally drain into IVC. Right counterparts of these vein drain directly into the IVC not in the right renal vein.



ADRENAL GLANDS

- Each gland is s/by superior, middle and inferior suprarenal arteries. Arterial supply is similar on both sides.
 - Superior SRA is a branch of inferior phrenic artery.
 - Middle SRA is a direct branch from aorta.
 - Inferior SRA is a branch of renal artery.

- V/D : Rt suprarenal vein drains directly into IVC while Lt suprarenal vein drains in left renal vein.
(Similarly right gonadal (testicular/ovarian) vein drains into IVC and Lt gonadal vein drains into the left renal vein)
- L/D : Drain into the lateral aortic nodes.

URETER

- N/s: - Sympathetic (T_{10} - L_1) parasymp. (S_2 - S_4)
- Length 25 cm. [Internal diameter 0.3 cm.]
- Lies behind gonadal and colic vessels in upper part but lower down it passes in front of ext. iliac / bifurcation of common iliac a.
- Lies anterior to genitofemoral nerve, psoas major
- Narrowest part of ureter is uretero-vesicle junction.
- Abdominal part of ureter: Anteriorly crossed by these structures.

On Lt. side	On Rt. side
Peritoneum	Peritoneum
Arteries (Lt. colic, gonadal)	Arteries (Rt. colic, ileocolic, gonadal)
Sigmoid colon and mesocolon	Root of mesentery + terminal ileum + 3rd part duodenum

Constrictions of U-

- Ureteropelvic junction
- Crossing of internal iliac a. at pelvic brim
- Ureterovesical junction (Narrowest part where ureter enters the wall of bladder)
- Juxta position of vas or broad ligament.
- Ureteric orifice

Referred pain of ureteric colic

Part of ureter	Located at	Referred to
1. Upper	PUJ	Testicles
2. Middle	Crossing of internal iliac a.	McBurney's point
3. Lower	-	Genital/ Perineal areas, sides of thigh/ groin (base of penis, labia, scrotum thigh)
4. Entire mural ureter	-	Strangury (painful & fruitless desire, to micturate)

- Ureter is contained in inter-sigmoid recess
- Retrocecal recess contain appendix.
- Spleen projects into greater sac.

URINARY BLADDER

• Trigone of UB :

- Ureters open in posterolateral angle, mucosa is smooth here
- Has interureteric crest forming base (*Bar of Mercier*)
- Mesodermal in origin.
- Posterior surface of UB is related to : Ureter, seminal vesicle, fascia of Denonvilliers, ampulla of ductus deferens.
- *Retzius cave* is a potential space b/w pubic bone & urinary bladder.

PROSTATE

- **B/s** : Supplied by inferior vesical, middle rectal and internal pudendal arteries (but NOT by external pudendal artery).
- **V/d**
Through plexus formed around sides and base of the gland. Valveless communication exist b/w prostatic and vertebral venous plexus (**Batson's plexus**), through which prostatic cancer can spread to vertebral column and in brain.

• Prostate has 5 lobes:

Lobe	Peculiarities/zone	Prone to
1. Anterior	No glandular tissue	-
2. Posterior	Peripheral zone, Carcinomatous transformation zone	M/c site of prostate cancer
3. Median	Periurethral/ central zone, Rich in glandular tissue	M/c site of BPH
4. Two lateral	-	Adenoma in elderly

- During prostatectomy both capsules are left behind.
- During thyroidotomy false capsule is left behind. Thyroid is removed along with true capsule as venous plexus lies deep to it.
- Prostatic venous plexus lies b/w true and false capsule.
- Prostate is separated from symphysis pubis through cave of Retzius (retropubic space)
- Posteriorly prostate is separated from rectum through fascia of Denonvilliers (rectovesical septum).

URETHRA : Male

- Urethra in male is 20 cm in length.
- Broadly divided into anterior & posterior urethra:
Anterior urethra includes : Penile & bulbar
Posterior urethra includes : Membranous & prostatic.

• Pre - prostatic part (1cm)

• Prostatic part (3cm)

Widest & most dilatable part. Closer to the anterior surface of gland. Prostatic gland's open through duct in posterior surface, opening is marked by urethral crests (verumontenum)/ medial longitudinal ridge of mucosa

• Membranous part

Shortest (1.5-2 cm), 2nd narrowest & least dilatable part of male urethra.

• Spongy/penile urethra

Longest part of urethra. Bulbourethral glands of Cowper's open into bulbar part of.

• External urethral meatus

Narrowest part.

Part	Transverse section	Epithelium	Remark
1. Pre-prostatic	Stellate (star shape)	-	-
2. Prostatic	Semilunar	Transitional	Most distensible
2. Membranous	Stellate	Pseudostratified columnar	M/c site of urethral ca
3. Bulbar	Transverse	-	Widest, M/c site of urethral injury/ stricture
4. Penile/ spongiose	Transverse	Pseudostratified columnar	Longest
5. External meatus	Sagittal	Stratified squamous	Narrowest

→ **Verumontenum or urethral crest** is a median longitudinal ridge of mucosa situated in the prostatic part of urethra.

→ **Colliculus seminalis** is an elevation in the middle of the urethral crest.

→ **Prostatic utricle** opens in this part (elevation) of prostatic urethra

Urethral Sphincters

	Internal (Sphincter vesicae)	External (Sphincter urethrae)
1. Nature	Involuntary	Under voluntary control
2. F/b/y	Smooth m/s	striated m/s
3. Surrounds	Neck of bladder and prostatic part urethra	Membranous urethra
4. S/b/y	Sympathatic fibres	S2- S4 parasymp. fibres

PERINEAL/GENITO-URINARY REGION

Penile Shunts

- Corporo-
 - glandular (Winter, Al Ghorab, Ebbehoy's)
 - spongiosal (Quakel or Sacher's)
 - saphenous (Gray hack's)
 - dorsal ven (Barry's)

Erection & Ejaculation

- Sensation from glans penis travel via pudendal nerve & integrated in sacral plexus.
- Parasympathetic activity (via NO release) is a/w erection.
- Sympathetic activity is a/w ejaculation.

Perineal Pouch/Spaces

	Superficial (SPP)	Deep (DPP)
1. Location	Superficial (inferior) to perineal membrane	Deep (but superior) to PM
2. Contents	1. Root of penis /clitoris (2 crura + bulb) 2. Superf. perineal m/s (Ischiocavernosus, Bulbospongiosus, Superficial transverse perinei) 3. Ducts of bulbourethral glands in males, [Greater vestibular glands & ducts in females] 4. Branches from perineal artery, 4 branches from artery of penis, Long perineal n, Posterior scrotal v/s and nerve	1. Membranous urethra 2. Deep perineal m/s (deep transverse perinei, sphincter urethrae) 3. Bulbourethral/ Cowper's glands in males 4. Dorsal artery of penis itself and stem of 4 arteries Dorsal n. of penis, branches from perineal nerve, Arteries & nerves to bulb of penis

- Superficial perineal muscles include superficial trans-perinei, bulbospongiosus & ischiocavernosus.
- RTA with pelvic injury involving bulb of penis, blood collects in superficial perineal pouch (butterfly hematoma).

Pubococcygeus

Its anterior fibres surround prostate in male & form **levator prostatae**. Fibres surround vagina in female & form **sphincter vaginae**.

Muscles attached with perineal body : are 9

- 3 unpaired: – External anal sphincter
- Bulbospongiosus
- Unstriated fibres of long coat of rectal ampullae of anal canal.
- 3 paired – Superficial transverse perinei.
- (Rt. & Lt.) – Deep transverse perinei.
- Levator ani
- (Pubococcygeus + Ileococcygeus).

Urogenital Diaphragm is composed of

- Deep perineal muscles (sphincter urethrae + Rt. & Lt. deep transverse perinei)
- Superior fascia of UGD.
- Inferior fascia of UGD (It forms perineal membrane)

Colles fascia is attached to anterior border of UGD & do NOT form part of it.

Pelvic Diaphragm is composed of

Coccygeus (ischiococcygeus) + *Levator ani* (-ilio & -pubo coccygeus)

VAGINA

- *Vaginal sphinctor is formed by*

1. Pubococcygeus (Pubovaginalis + pubourethralis)
2. External urethral sphinctor
3. Urethrovaginal sphinctor
4. Bulbospongiosus

There is no internal urethral sphinctor in female GUT. But it is presents in males at the bladder neck/proximal urethra. It prevents retrograde ejaculation of semen.

- *Vaginal mucosa is lined by* --- stratified squamous non-keratinized epithelium.
- There are no glands in the vaginal lamina propria and vaginal lubrication is provided by transudate from the blood vessels as well as by secretions of the Bartholin's and Skene's glands.
- *The Bartholin's glands* (also called greater vestibular glands) are two glands located slightly posterior and to the left and right of the opening of the vagina. They secrete mucus to lubricate the vagina and are homologous to bulbourethral glands in males.

Bulbourethral and Bartholin's gland

	Bartholin's /Greater vestibular gland	Bulbourethral glands of Cowper
1. Found in	Female	Male
2. Location	Superficial to perineal membrane in SPP	Deep to perineal membrane in DPP
3. Duct opens in	Vagina (postero-lateral part)	Penile (spongy) part of urethra
4. Function	Helps in lubrication of lower vagina	---
5. Applied	Infected in Gonorrhoea	---

- **Gartner's** cyst arises from remnants of mesonephric duct. it lies in the anterolateral vaginal wall.
- 'Clue cells' are seen in vagina in bacterial vaginosis.
- Blood supply :
Vaginal br. of uterine a. or internal iliac artery → Whole vagina
Vaginal br. of inferior vesical artery → Anterior vagina
Internal pudendal artery → Caudal (posterior) vagina

FALLOPIAN TUBE (Uterine tubes/ Oviducts)

- Length is 10 cm (~ 4 inches)
- M/c site of ligation during tubal ligation—isthmus
- Fertilization occurs in—Ampulla
- Tubes are m/c site of ectopic . M/c site of ectopic pregnancy in FT—**Ampulla** > isthmus
- Tubes are lined by—**Ciliated columnar epithelium**
- 'Peg cells' are seen in fallopian tubes.

SCROTUM & TESTES

- Volume of testes before puberty < 1.5 or 2 mL.
- Volume of testes after puberty 6-9 mL.
- The mean scrotal temperature is 2.5 °C less than body temperature. A normal body temperature of 98.6 °F lowers sperm counts and prevents sperm from maturing normally.

GLUTEAL REGION

- **Gluteus maximus** is strong extensor of hip --- It is s/by **inferior gluteal nerve** (L5,S1,S2)
 [Mnemonic: Glue mein hai maximum info]

- Gluteus medius, gluteus minimus and tensor fasciae latae are s/by **superior gluteal nerve** (L4 L5 S1), which arise from sacral plexus.
- Gluteus medius and minimus abduct the thigh at hip joint .Paralysis or weakness of these m/s or nerve produces +ve Trendelenberg's sign and lurching gait.
- Both superior and inferior gluteal nerves enter the gluteal region through greater sciatic foramen.
- Superior gluteal artery supply --- gluteus medius.
- Gemellus superior and obturator internus are s/by **nerve to obturator internus** (L5,S1,S2).
- Gemellus inferior and quadratus femoris are s/by **nerve to quadratus femoris** (L4 L5 S1).

[Readers can refer VDA's anatomy charts for pictorial and simplified depiction of all these nerves]

- When bilateral glutei medius and minimus are paralyzed waddling gait is seen
- Preferred site for i.m. injections is anterosuperior quadrant (in the glutei medius and minimus)
- When the gluteus maximus is paralyzed as in muscle dystrophy, child stands up from a sitting posture by supporting their hands on legs (Gower's sign)
- Best muscular site for DPT injection in a newborns is --- vastus intermedius

LOWER LIMBS

Popliteus

- Referred to as key to the knee joint as it unlocks a locked knee joint.
- Takes origin from anterior end of the popliteal groove on the lateral condyle of femur. Its origin is tendinous & is **intracapsular**.
- At origin it is attached to the back of lateral meniscus.
- Tendon expands in a triangular fleshy belly, which is inserted on the posterior surface of tibia above the soleal line.
- Rotates the tibia medially on the femur.
- Flexor of the knee joint.
- Protects lateral meniscus from injury.

HISTOLOGY

GIT

- Parasympathetic nerves (like Auerbach) stimulate peristalsis but inhibit sphincters.
- Myenteric plexus of Auerbach's*
Contains parasympathetic ganglia b/w circular and longitudinal m/s coats. It is present in whole GIT from esophagus to colon
- Sympathetic nerves are motor to sphincters and to the muscularis mucosa and ↓ the peristalsis.*

Peyer's Patches

- Present mainly in ileum along anti-mesenteric border.
- GALT (Gut Associated Lymphoid Tissues) are found in **mucosa** of intestine. They become numerous lower down in S.I. (*Abundant in terminal ileum and absent in jejunum*)
- Peyer's patches are ulcerated in typhoid fever forming oval ulcer along the long axis of bowel (so no strictures).

- Glands of Brunner & crypts of Lieberkuhn both secrete mucous/mucin.
- Crypts of Lieberkuhn are dips of columnar epithelium found in whole length of small intestine.
- Glands of Brunner's are found in sub-mucosa of duodenum.
- Peyer's patches are lymphoid aggregates mainly found in terminal ileum along anti-mesenteric border. Secrete IgA.
- Paneth cells are found only at the bases of crypts. Probably they secrete lysozyme and guanylin (Role in mucosal immunity). They do not reach upto the epithelium.
- Goblet cells are mature mucous cells. They are present in stomach, intestine, trachea, etc.

Characteristics of large intestine

- No villi but only glands are present (crypts) containing high proportion of goblet cells.
- Presence of haustrations, taenia coli, appendices epiploicae** (these 3 characteristics of large intestine are *absent in rectum*).
- Taenia coli* are 3 ribbon-like bands formed by longitudinal m/s coat of large intestine. Proximally they converge at the *base of appendix*.
- Appendices epiploicae* are bulbus pouches of peritoneum distended with fat (**peritoneal mice**), project from serosa of sigmoid colon (**most numerous**) and posterior surface of transverse colon (*Absent in appendix, caecum and rectum*). Mucosal hernia a/w this, may result in diverticulosis.

- Amino acids are absorbed from ileum and distal jejunum
- Oligopeptides like di & tri-peptides are absorbed from duodenum and prox. jejunum.
- Fat (& long chain FA) are absorbed from jejunum.

Permanent mucosal folds of GIT

These folds are not obliterated by distension

- Plicae semilunaris (valvulae conniventes or valves of Kerkring)* are circular folds of mucosa of small intestine. present in 2nd part of duodenum + jejunum + proximal ileum. The absorptive surface of small intestine is multiplied by these folds, which project into the lumen. In intestinal obstruction valvulae conniventes of jejunum are seen on X-ray.
- Spiral valve of Heister* is found at the opening of cystic duct into the common hepatic duct to form the CBD.
 - It is not a true valve but is permanent and narrows down the lumen of cystic duct at the terminal end.
 - When the duct is distended, the spaces between the folds get dilated, making the folds more obvious.
- Transverse/horizontal rectal folds* --- Houston's valves or plicae transversalis.

Temporary mucosal folds of GIT

These folds disappear on distension

- Gastric Rugae
- Longitudinal rectal folds.

Glands of skin

1. Sweat glands

1. Typical sweat glands:

Secretion is of *eccrine or merocrine variety*. Deliver watery secretion to surface by exocytosis, cell is intact. Greatest concentration on thick skin of **palm/ sole**, face including forehead. *Not found on margin of lips, glans penis and tympanic membrane*. They are distributed all over the body (except for the lips, tip of penis and clitoris) although their density varies from region to region. Humans utilize eccrine sweat glands as primary form of cooling.

2. Atypical/modified sweat glands:

They have apocrine glands. Apical part of cell break and discharge. Apocrine sweat glands are limited to axilla (armpits) and perianal areas in humans, ceruminous, ciliary glands (glands of Moll) of eyelids. Ceruminous glands, which produce ear wax, and mammary glands, which produce milk are true apocrine glands.

2. Sebaceous glands

Confined to nonhairy skin Eyelids, lips, papillae of breast, labia minora (**absent on palms and soles**).

Secretions are holocrine means whole cell disintegrate

- Ceruminous glands and ciliary glands (glands of Moll) of eyelids are modified sweat glands of apocrine variety.
- Meibomian glands are modified sebaceous glands.
- Sweat glands are innervated by cholinergic nerves and have contractile myoepithelial cells which help in expressing out their secretions.
- Collateral circulation is well established in skin.

- Columnar epithelium have absorptive property: So prevalent in GIT.
- Fallopian tubes are lined by ciliated columnar epithelium. The ciliated cells are most abundant at the fimbriated end
- Ducts of Bellini are found in kidney
- In esophagus toughest layer is muscularis externa, serosa is nearly absent.
- In small intestine submucosa is toughest layer.
- Space of Disse, Kupffer cells, Ito cells & cords of Billroth are seen in liver.
- Simple squamous epithelium is found lining areas where passive diffusion of gases occur: e.g. walls of capillaries, linings of the pericardial, pleural, and peritoneal cavities, as well as the linings of the alveoli of the lungs.
- Olfactory epithelium is superior to superior turbinate of nose.

EPITHELIUM

Type of	Subtype	Found in/ Forms lining of
c Squamous	Simple	Blood vessels (endothelium), Linings of alveoli, cavities, lining of serosa (pericardium, mesothelium of pleura, peritoneum), Bowman's capsule, thin segment of LOH
	Stratified, Non-keratinized	Vagina, upper aero-digestive tract (mouth, tonsils, pharynx, VC, esophagus), cornea
	Stratified, keratinized	Skin, Duct of sebaceous glands, Anus below Hilton's white line
c Columnar	Simple, non-ciliated	Mucosa of Stomach, intestine, Gall bladder, cervical canal
	Ciliated	Uterus, fallop tubes, endocervix, eustachian tube, middle ear, Respiratory epithelium
	Pseudostratified, ciliated	Upper 1/3 rd of nasal cavity (Olfactory epithelium), Respiratory epithelium [Lower 2/3 rd of nasal cavity, auditory tube, trachea, bronchi, respiratory tract upto bronchioles] Ductus deferens
	Pseudostratified, with stereocilia	Epididymis
c Cuboidal	Simple	Terminal bronchioles, alveoli, Germinal epithelium
	Stratified	Ducts of many glands (pancreas/salivary glands/sweat glands), lining of Bartholin glands [NOT in sebaceous gland]
c Transitional epithelium	(Urothelium)	Urinary passage (from minor calyces, renal pelvis → ureter → UB → prostatic urethra)

EMBRYOLOGY

Events after fertilization

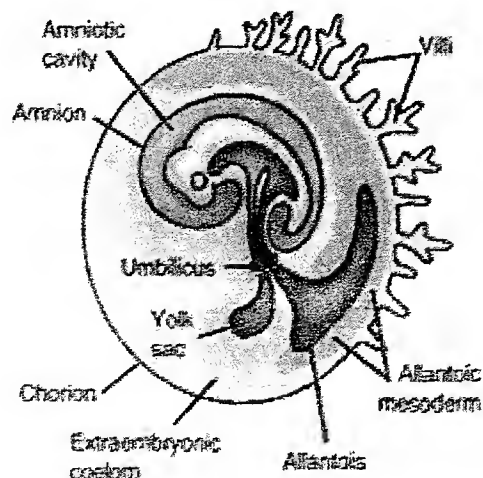
Time	Event
- 24 hour	Ovulation (occurs 24 - 36 hours prior to fertiliza ⁿ)
0 hour	Fertilization (in the ampulla of fallopian tube)
30 hour	Blastomere (two cell stage, still covered by ZP)
day 3-4	Morula (16 cell stage) is formed. Inner cell mass and outer cell mass are distinct
day 4	Morula enters uterine cavity
day 5	Blastocyst formed
day 5-6	Zona pellucida is shed off, Blastocyst hatches out → naked blastocyst is ready for implantation
day 6	Implantation starts (Blastocyst attaches to the endometrium). It occurs in posterior wall of the body of uterus close to fundus. It corresponds to day 20 of a regular menstrual cycle.
day 8	Bilaminar germ disc is formed
day 9	Primary yolk sac
day 10	Conceptus completely embedded in the endometrium
day 13,14	Primary chorionic villi formation starts (primitive streaks), secondary yolk sac chorion frondosum is formed at the embryonic end which contributes in the formation of placenta
day 21	Feto placental circulation established, tertiary villi formed
day 12-20	Trilaminar germ disc
During 3rd wk	Most characteristic events is gastrulation which establishes formation of all 3 germ layers
day 22-23	Neural tube formation begins (Notochord)

Events occurring in 3rd week of IUL

- **Gastrulation:** Establish all 3 germ layers (14-16 days).
Embryonic disc with 3 germ layers is formed at 3rd wk of gestation.
- Primitive streak formation starts.
- Notochord formation
- Body axis establishment : Ant, post, dorsal, ventral etc.

- Oocyte is viable for 24 hrs after its liberation. Most human sperms can survive for a period of 48 hours in FGT.
- Zona pellucida sheds off in blastocyst stage
- Implantation occurs in blastocyst stage (Trophoblast cells of blastocyst attach to endometrium and ZP is shed off). In human implantation is of interstitial type.
- Fertilin, a protein found on surface of sperm head, helps in penetration of sperms through ZP and it prevents polyspermy.
- Placental trophoblasts do not express polymorphic HLA class -I and II.

- **Capacitation:** Physiological & biochemical changes for functional maturation of the spermatozoon (Removal of glycoprotein coat, interaction of fertilizin derived from ovum and antifertilizin derived from sperm) in FGT before fertilization. These changes enables them to penetrate and fertilize an ovum. This results in **hyperactivation**, which is c/by pronounced flagellar movements, marked lateral excursion of the sperm head and a non linear trajectory.
- **Acrosome reaction** confers on spermatozoa the ability to penetrate the zona pellucida by binding ZP3 receptors. followed by lysis by acrosomal enzymes (*acrosin or zonalysin, esterases and neuraminidases*).
- Embryonic period is from 3rd to 8 wks post fertilisation.
- Zygote is called up to 9 days.
- Embryo is called up to 9 wks.
- Amnion is the innermost layer facing fetus.



- **Malformation** is primary structural defect of an organ
- **Syndrome** is a combination of multiple malformations thought to be pathogenitically related and not representing a sequence.
- **Deformity** is abnormal position or abnormal form of a body part.

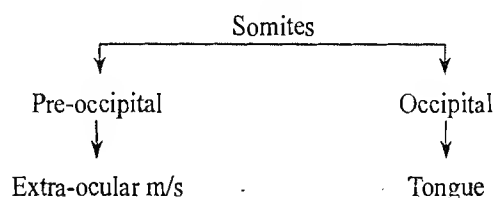
Ectoderm

- Fate of entire ectoderm depends upon BMP (bone morphogenetic protein) concentration
High levels → Results in epidermis formation
Low levels → Induces neural crest
BMP inhibition (by Noggin, follistatin, chordin) → Neural plate formation

Mesoderm

Intraembryonic mesoderm is formed by proliferation of cells of **primitive streak**. Divided in 3 parts

1. Paraxial mesoderm → somatomes → somities



- Dermatome → Dermis
- Myotome → Muscles
(e.g. smooth m/s of dorsal aorta)
- Sclerotome → Vertebral column (centrum of vertebrae), ribs.

2. Lateral plate mesoderm
3. Intermediate mesoderm.

- Primitive streak remnants give rise to sacrococcygeal teratoma.
- Neural tube completely closes at 20 days.

NOTOCHORD

- Defines the axis of the embryo and gives it some rigidity
- Serves as the basis for development of axial skeleton.
- It indicates the future site of vertebral bodies. After the development of vertebral bodies, the notochord degenerates and disappears but persists as the nucleus pulposus of the IVD.

- It functions as the primary inducer of overlying ectoderm to develop into neural plate.

Descent of Testis

Develops from coelomic epithelium of mesonephros from T10 - T12 level

Months of intra uterine life	Location of testes
2 nd month	Begins to descent
3 rd month	Reaches iliac fossa
4 - 6 month	Rests at DIR
During 7th month	Traverse inguinal canal
During 8th month	Reaches SIR
End of 8th month	Reaches scrotum
9 month	Reaches bottom of scrotum

- Testes descends into scrotum at the end of 8th month.
- Kidney ascends from iliac fossa to lumbar region

Aortic Arch Derivative

See diagram in pharyngeal arches section.

7th Cervical intersegmental a. : Axis a. of upper limb is formed
:- Subclavian a. → Axillary → Brachial Ant. Interosseus → Median a. → Deep palmar arch.

Remnants of axis artery of upper limb

Axillary artery, brachial artery, anterior interosseous artery, median artery.

Remnants of axis artery of lower limb

Inferior gluteal artery, companion artery of sciatic nerve, popliteal artery, peroneal artery

FETAL CIRCULATION

There are 3 shunts or bypass channels in fetus (DV, FO and DA) and 3 vessels connecting to placenta (2 A + 1 V)

Sequences of Post natal events

Clamping → Interruption of umbilical cord
↓
Physiological closure of DV and umbilical vessels
↓ pulmonary vascular resistance and ↑ SVR
↓
Functional closure of DA (10-15 hrs)
↓
Anatomical closure of DA (by 2-3 wks)
↓
Anatomical closure of DV & umbilical v/s (by 2-3 mo.)
↓
Functional closure of foramen ovale (by 3 mo.)
↓
Anatomical closure of FO (by 6 mo.)

Fate of fetal shunts

Lt umbilical vein becomes → Ligamentum teres
FO is replaced by → Fossa ovalis

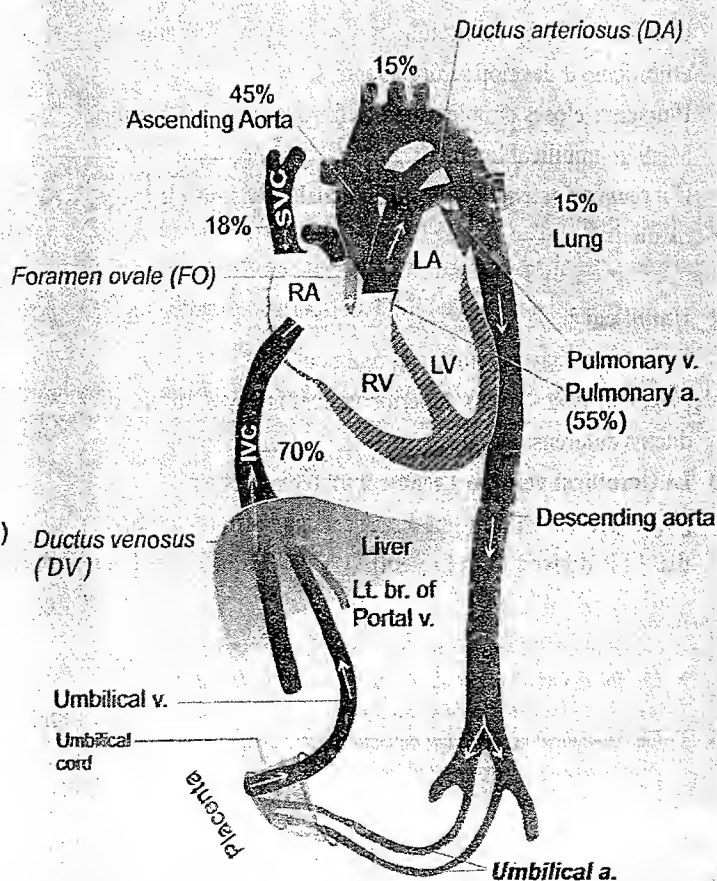
DA becomes Ligamentum arteriosum

DV becomes Ligamentum venosum

Umbilical arteries

Proximal part becomes → Sup. Vesical arteries

Distal (obliterated part) forms → Lateral umbilical ligament



- Double aortic arch is d/to persistence of rt 4th arch or when both 4th arches & dorsal aorta remain present.
- A persistent Lt SVC usually drains into the --- coronary sinus
- Supra cardinal & subcardinal veins are involved in formation of IVC.
- Patent FO (foramen orale) is d/to failure of fusion of ostium primum with ostium secundum.

- In embryo, at 4 months there are:-

2 umbilical arteries

1 umbilical vein (left sided)

- After birth :-

1. Left umbilical vein forms → Ligamentum teres hepatis
2. Ductus venosus → Ligamentum venosum
3. Vitelline veins → Hepatic vein, IVC (inf portion), portal vein, SMV

Fetal Post-natal derivative / Remnants

- Allantois → Urachus → Median umbilical Ligament

- Urachus

Urachus is a connecting tube b/w developing UB and the umbilicus. It develops from allantois.

If urachus closes or obliterates as fibrous band → Forms Median umbilical ligament

If it remains patent → Forms urachal cyst/ sinus/ urinary fistula

- Umbilical a.

Distal part - lateral umbilical ligament.

Proximal part - forms superior vesical artery & artery of ductus deferens in males.

- Lt Umbilical vein → Ligamentum teres of liver

[N.B. : Left is left & right disappears and also remember that Lt is derived from Lt vein]

- Umbilical cord contains — 2 A + 1 V (i.e. right and left umbilical arteries and only left umbilical vein)
- Fetal umbilical vein & adult pulmonary veins are the only veins which carry purely oxygenated blood.

- Ant. cardinal vein - Lt. → Oblique vein of Marshall → Opens directly in RA.
- Vitelline & Umbilical veins → sinusoids of liver, hepatic vein, portal vein.
- On each side int jugular and subclavian veins unite to form

ant. cardinal v. and from lower limb & pelvis int. & ext. iliac veins form post cardinal v. into which drains segmental cardinal V. (intercostal and lumbar). The two cardinals unite to form common cardinal vein (The duct of Cuvier).

- Foramen caecum - Thyroid gland
- Lingual swelling - Tongue
- Ventral Pancreatic bud :- Lower part of head of pancreas + Uncinate process
- Dorsal pancreatic duct - Rest of pancreas (upper part of head)

DERIVATIVES OF MESENTERIES OF FOREGUT

- By the 5th week of development liver, pancreas (ventral bud), GB have developed in ventral mesogastrium. The spleen and dorsal pancreatic bud have developed in the dorsal mesogastrium.

- Ventral mesentery / mesogastrium

It is a part of septum transversum and is divided by developing liver in 2 parts

- Dorsal part --- Lesser omentum
- Ventral part --- Falciparum ligament, Coronary ligament, Triangular ligament

- Dorsal mesentery / mesogastrium

Development of spleen modifies dorsal mesogastrium (mesentery of stomach) and divides it into 3 parts

- Cranialmost part --- Gastrophrenic ligament
- Cranial part --- Gastrosplenic ligament, --- Lienorenal ligament,
- Caudal part --- Greater omentum

Anomalies of rotation and fixation of gut

- Non-rotation

Failure of rotation of the midgut results in location of small intestine on the right side and caecum and ascending colon on the left side

- Mal-rotation / Incomplete rotation

Affects the duodenojejunal segment and the caeco-colic segment. Ladd's band may be present and the caecum may be placed in midline below the stomach. Malrotation may be a/w midgut volvulus and it is a acute surgical emergency.

- Reverse -rotation

Superior mesenteric artery goes behind 3rd part of duodenum and transverse colon is behind the SMA.

• Anomalous fixation of mesentery

Results in excessive mobility of different part of guts.
Volvulus and torsions may result.

- The *physiological hernia* occurs at 6th week. At 10th week the derivatives of midgut loop return back to the abdominal cavity. This is called as reduction of physiological hernia. This is becoz of the growth of the abdominal cavity & the relative ↓ in the size of liver.

• Derivatives of the primitive gut & their blood supply:

Gut	Derivative	Blood supply
• Foregut	Whole gut proximal to caecum	Coeliac artery, SMA
• Midgut	Ascending colon + proxm 2/3rd of trans. colon	SMA
• Hindgut	Distal 1/3rd of trans. colon + Descending colon, rectum	IMA

Development of Tongue

• Epithelium

1st arch (mandibular nv) → Ant 2/3rd

3rd arch (9th nv) → Post 1/3rd

4th arch (vagus) → Posterior most part

- Occipital myotomes → Muscles
- Mesenchyme → Connective tissue
- Tuberculum impar → Pre-sulcal mucosa
- Hypobranchial eminence → Post-sulcal part

Thyroid gland

- Develops from a median endodermal thyroid diverticulum at caudal end of thyroglossal duct.
- Lateral thyroid develops from - 4th pharyngeal pouch.
- Position of upper end is marked by **foramen caecum**.
- Parafollicular cells (C-cells) develop from ultimobranchial body (5th pharyngeal pouch).

Neural Crest derivatives

- Neurons of *sensory* ganglia of 5, 7, 8, 9, 10 (remember 5 to 10 except 6).
- Neurons of *sympathetic* ganglia and DRG (Spinal posterior nerve root ganglia)

- Adrenal Medulla (Chromaffin cells / tissue)
- Melanoblasts
- Schwann cells, somatomeres
- Corneal stroma and endothelial cells
- Mesenchyme of dental papilla and **odontoblast**
- *Pia & arachnoid mater.*

→ Inner cell mass forms the embryonic disc

→ Somites develop from paraxial mesoderm.

→ All connective tissues of the body (bone, blood, cartilage) develop from mesoderm.

→ Notochord develops in 3rd week.

→ Cauda equina is derived from neural tube not from neural crests.

NEURAL TUBE

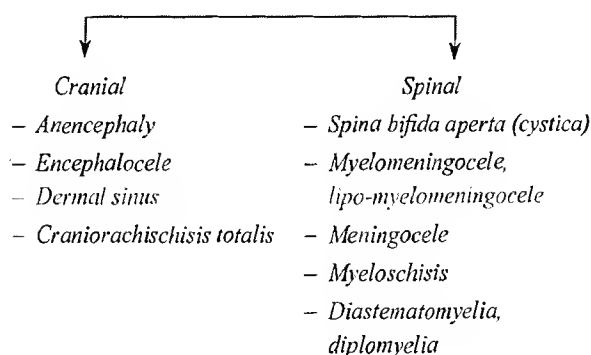
- Neural tube is formed by two distinct processes. i.e. primary and secondary neurulation or canalization
- Neural tube closure starts from cranial region
- Anterior and posterior neuropore are most vulnerable to defects because they close at the last. Neural tube defects (NTDs) result from failure of fusion of these neuropores.

Neural tube defects (NTDs)

- NTDs are of 2 types

1. Open NTDs : Involve entire CNS. A/w hydrocephalus and Chiari II malformations. Defect is d/to defective primary neurulation. CSF leak is usually seen.
2. Close NTDs : Usually involve spine. results from defective secondary neurulation. Defect is fully epithelialized.

- NTDs have either cranial presentation or spinal presentation



Embryological Defects in Cardiac anomalies

Anomaly	Cause	Components
TOF	Unequal division of conus resulting from anterior displacement of conotruncal septum	PS + RVH + VSD + Overriding of aorta
Persistent truncus arteriosus	Conotruncal ridge fails to fuse & to descend towards ventricle	PA arises from undivided truncus + VSD + Common truncus receives blood from both the ventricles
TGA	Conotruncal septum fails to follow its normal spiral course & runs straight down	Aorta arises from RV + Pulmonary artery arises from LV + PDA

Important derivatives of three germ layers

	Flattened cells Inner cell mass	Columnar cells of Inner cell mass	Trophoblast cells
	↓	↓	↓
	1st germ layer	2nd germ layer	3rd germ layer
	↓	↓	↓
	Endoderm	Ectoderm	Mesoderm
Eyes, ear	-	1. Lens, 2. Iris m/s (sphincter/ dilator pupillae) 3. Retina 4. Membranous labyrinth	1. Ciliary m/s 2. Sclera, choroid, vitreous 3. Stroma of cornea 4. Lids m/s
CNS		Brain, neural crest	Dura mater
Pharyngeal Pouches		Clefts	Arches
Resp	Respiratory tract		
CVS			Whole CVS, blood, BM, mesenchyme, mesothelium, monocyte derivatives
Skeleton			Whole skeleton, Bony orbit
GIT	1. Epithelium of whole g.i.t. 2. Liver, GB, ducts & acini of pancreas		1. LN & Spleen
GUT	Urethra, UB, Lower vagina		Trigone of bladder
Glands	Most endocrine glands,	Adrenal medulla, pituitary	Adrenal Cortex

[Development of structures of eye are described in Ophthalmology section]

- The proximal 2/3rd of trans. colon develops from midgut and artery of midgut is sup. mesenteric a.
- All muscles (skeletal, smooth, cardiac) are mesodermal in origin except muscles of iris (sphincter and dilator pupillae) which are neuroectodermal in origin.

Paramesonephric (Mullerian) ducts

- Invagination of coelomic epithelium in females forms → genital ducts (Mullerian ducts).
- Lies lateral to mesonephric ducts & development of P ~ predominates (female pattern) over mesonephric ducts development. P ~ regress only in response to MIS.
- Cranial part → Fallopian (uterine) tubes
- Caudal part → Uterus & cervix → Uterovaginal canal → Vagina (upper 4/5th)
- Mullerian eminence → Hymenal orifice.
- Hydatid of Morgagni (HM)
- Caudal part + phallic UGS → vestibule
- P ~ ducts in male forms remnants
 - Appendix of Testis (attached to upper pole) (T_A)
 - prostatic utricle (or utriculus masculinus) (U_P)

[Mnemonic : $H_M T_{And} U_P$ from para]

- The imperforate hymen is the result of failure of fusion of central part of Mullerian eminence to disintegrate.

Mesonephric duct : Derivatives

Preceding structure	In Males	In Females
Ureteric bud forms →	Collecting part of kidney (CT, calyces, pelvis, ureter)	Collecting part of kidney (CT, calyces, pelvis, ureter)
In UB	Trigone	Trigone
Urethra	Above the opening of ejaculatory ducts	Posterior wall
Ejaculatory system	Seminal vesicle + ejaculatory duct, Vas deferens, epididymis	Broad Ligament & para ovarian cyst (Gartner cyst)
Mesonephric tubules (cranial end)	Remnants are formed epigenital tubules, Appendix of epididymis	Epoophoron/ Organ of Rosenmüller
Mesonephric tubules (caudal end)	Paradidymis	Paroophoron

REMNANTS:

- *Gartner's duct* (Wolffian duct) is the remnant of mesonephric duct. The duct sometimes forms a cyst in the broad ligament called Gartner's cyst.
- *Organ of Rosenmüller* is a remnant of caudal part of epophoron/paro-phoron.

Derivatives of Indifferent Gonads/Genital ridge (Genital glands)

Muscles	Male	Female (Homologous structure)
• Indifferent gonads/ Genital glands	Testes	Ovary
• Gonadal ridge cortex	Seminiferous tubules	Ovarian follicles
• Mesenchyme of gonadal ridge	Cells of Leyding	Theca cells
• Coelomic epithelium cells	Sertoli cells	Follicular cells
• Sex cords	Seminiferous tubules	Pfluger's tubules
• Genital tubercle	Penis (C. cavernosa)	Clitoris
• Urogenital folds	Penile urethra (C. spongiosa)	Labia minora
• Genital (Labioscrotal) swellings	Scrotum	Labia majora
• Gubernaculum	Gubernaculum testes	Round lig. of uterus, Ligament of ovary

Derivatives of Urogenital Sinus (UGS)

	Male	Female
• Ventral and pelvic part	UB, Prostatic urethra	UB, Whole urethra
• Phallic / urethral part	Prostatic urethra (Infra montanal part)	Vagina : vestibule
• Glands	Bulbourethral glands	Greater vestibular (Bartholin) glands
• Sinovaginal bulb	Part of prostatic utricle	Vagina (lower 1/5th)

- Primitive gonads arise from the genital ridge on each side near the adrenal glands.

Development of vagina:

According to one theory its upper 1/5th develops from the mesoderm of UVC (uterovaginal canal) & the lower 2/5th develops from the endodermal vaginal plate (UGS → SVB → Lower 2/5th of vagina).

Another theory is that :

Endoderm → UGS → SVB → Epithelium of entire vagina.

The central part of Mullerian eminence degenerates to form hymenal orifice & the peripheral part is retained as the hymen.

BRANCHIAL/ PHARYNGEAL APPARATUS**Branchial apparatus consist of :**

1. Branchial clefts derived from **ectoderm**
 2. Branchial arches derived from mesoderm + neural crests
 3. Branchial pouches are endodermal in origin.
- M/s of the arches are s/by nerve of that arch. (This is also an easy way to remember nerve supply of all these muscles).

Branchial/Pharyngeal Arches

- The pharyngeal arches are bilateral/paired swellings that surround the foregut of the embryo. They are wedged b/w the developing heart and brain. Pharyngeal arches develop in a **rostral to caudal** sequence.
- The components of each pharyngeal arch include an aortic arch, a specific cranial nerve and associated muscle, and a cartilage skeleton.
- The first, second & third arch contribute to the structures above the larynx, while the last 4th & 6th arch contribute to the larynx & trachea.

Branchial/Pharyngeal Clefts

- Occasionally, pharyngeal membrane rips and forms what is essentially a gill slit (pharyngeal cleft) b/w two pharyngeal arches. If the slit does not close, it may form a tract (fistula) from the pharynx to the outside of the neck.
- Ventral part of 1st cleft is obliterated. Dorsal part forms epithelial lining of EAM (external auditory meatus).
- Pinna is formed from series of swellings / hillock that arise on 1st & 2nd arches + 1st cleft.
- 2nd arch grow faster & overhangs 3rd, 4th, 6th arches & is called cervical sinus.
- Cavity of cervical sinus is normally obliterated. Persistent cervical sinus can lead to → branchial cyst.

BRANCHIAL/ PHARYNGEAL ARCH DERIVATIVES

Arch	Corresponding Aortic arch derivatives	Nerve	Muscles	Structures formed by cartilage of the arch
1st (Mandibular arch)	Maxillary artery, ECA	Mandibular, Chorda tympani	M/s of mastication, Anterior belly of digastric, TT, TVP, mylohyoid	Meckel's cartilage ↓ Malleus, incus, Mandible, Spheno-mandibular ligament
2nd (Hyoid arch)	Stapedial artery	Facial	M/s of facial expression, [Occipito-frontalis, platysma, posterior belly of digastric, stapedius, Auricular m/s	Reichert's cartilage → 5'S Stapes Styloid process Stylohyoid ligament, Smaller/lesser horn (cornu) of hyoid Superior half of hyoid
3rd	CCA Prox. part of ICA.	Glossopharyngeal (IX)	Stylopharyngeus	Greater cornu of hyoid Lower half of body of hyoid, Thymus
4th	Lt : Aortic arch Rt: Proximal part of Rt SCA	Vagus (X), SLN	M/s of pharynx, crico, & LVP	Laryngeal cartilages (Thy, Epi, Cu)
5th	Disappear	Disappear		
6th	Lt : Pulmonary artery (prox part) Rt: Ductus arteriosus & pulmonary artery	Vagus (X), RLN	All intrinsic m/s of larynx except cricothyroid	Laryngeal cartilages (Ary, Co), cricoid & tracheal cartilages

Pharyngeal Pouches

- Endoderm lines the internal (foregut) surfaces of the pharyngeal arches. The endodermally lined depressions b/w the pharyngeal arches are called pharyngeal pouches.

Pouch	Part	Derivative
5th	Ultimobranchial body →	Parafollicular/C-cells of thyroid
4th	-	Superior parathyroids
3rd	Dorsal wing	Inferior parathyroids
	Ventral wing	Thymus
2nd	Ventral	Epithelium of palatine tonsil
	Dorsal	Tubo-tympanic recess
1st	Dorsal	Tubo-tympanic recess → Eustachian tube (proximal part), Middle ear cavity (distal part)
	Ventral	Obliterated

- Remember that superior parathyroid glands develop from 4th pouch [Tips: 4 is superior number than 3] & inferior parathyroids from 3rd.
- Caudal-pharyngeal complex is formed by 5th + some element of 4th pouch.

- Branchial cyst. & fistula develop from vestigial remnant of 2nd branchial cleft.
- Branchial fistula/sinus passes between two carotids (i.e. ICA & ECA)
- Incomplete closure of ectodermal clefts is known to cause --- coloboma of iris and retina. Epiglottis develops from the hypobranchial eminence

- Structures fully developed at birth
(Attains adult size at birth)
Mastoid antrum, tympanic cavity, ear ossicles, structures of internal ear.

- Structures less developed at birth
Bony external ear canal, mastoid process and mastoid air cells (which are pneumatized by 6th yr), Maxilla
- Structures which are *not* developed or not present at birth
Otic capsule, petrous temporal bone

LARYNGEAL CARTILAGES

- At the level of thyroid cartilage
Carotid pulse is palpable, Bifurcation of CCA
- At the level of cricoid cartilage
Cricothyroidotomy is done in the space b/w cricoid and thyroid cartilages.
- In high tracheostomy incision is given just above the isthmus in 1st tracheal ring.
- In low tracheostomy incision is given through 2nd - 4th (or 2-5th) tracheal rings.
- During emergency intubation cricoid cartilage is pressed (Selick's maneuver).

PROCEDURES

- Needle biopsy of liver
 - The biopsy is typically performed in the 7th or 8th intercostal space in mid axillary line, but location may vary. The biopsy should be performed in an intercostal space which is dull to percussion at the end of exhalation.
 - Highest intercostal space which can be used for liver biopsy is 7th ICS. Above this level lung may be injured.
 - Misplaced needle could damage kidney, colon or pancreas and may cause pneumothorax.
- Paracentesis thoracis
 - Is drainage of pleural fluid (in pleural effusion) from pleural space
 - Appropriate sites for insertion of a chest drain are
 - a. 5th ICS in the mid-axillary line → Fluid
 - b. 2nd ICS in mid-clavicular line → Air
- Needle decompression of the pleural space
 - Done in tension pneumothorax
 - A large gauge needle is inserted through 2nd ICS

- Pericardiocentesis
 - Decompression of cardiac tamponade / pericardial effusion
 - Needle is inserted via left costo-xiphoid angle at 45° or by parasternal route through left 5th intercostal space.
- Intraosseous Canulation
 - M/c site is proximal tibia
 - A large bore needle is inserted 2 cm distal and slightly medial to tibial tuberosity at an angle of 90°
- To decompress hydrocele needle is inserted between two layers (parietal and visceral layers) of tunica vaginalis.
- Testicular biopsy : Main indication for diagnostic testis biopsy remains to distinguish b/w obstructive and nonobstructive causes of azoospermia. Testis biopsy is absolutely indicated for the well-androgenized azoospermic man with normal size testes, normal or minimally elevated FSH and no evidence of retrograde ejaculation in the postejaculatory urine.
- During lumbar puncture needle is inserted upto subarachnoid, but it does not pierce posterior denticular ligament.
- Neurovascular bundle of each intercostal space lies in groove of lower border of rib. So while doing pericardiocentesis, or intercostal chest tube placement needle is inserted close to upper border of rib.
- During left anterior small thoracotomy, pleural space is approached from left and care is taken not to damage the internal mammary artery, which runs 1-2 cm lateral to left sternal border.

SOME HIGH YIELD POINTS

VARIOUS APPROACHES IN SURGICAL ANATOMY

Procedure	Approach
• Drainage of axillary abscess	Floor of axilla
• Laparotomy in blunt trauma abdomen	Midline incision
• Sx for thoracic extension of cervical goitre	Neck
• Thoracotomy	Lateral

- Traube's area - tympanic note of fundus of stomach is percussed here.
- Aortic knuckle - in PA view of CXR arch of the aorta is seen as a projection beyond the left margin of the mediastinal shadow, which is called aortic knuckle.

- Vitelline vein gives rise to --- hepatic v., portal v.,

sinusoids.

- Policeman of abdomen is --- greater omentum
- Abduction at Hip joint is caused by gluteus medius, minimus, tensor fascia latae, sartorius.
- *Fabella* : is a small sesamoid bone present in the tendon (origin) of Lateral head of gastrocnemius.

Brodie's bursa : Lies deep to the medial head of gastrocnemius (and also deep to semimembranosus).

Baker's cyst : is median posterior swelling (as opposed to the more medial semimembranosus cyst) in the popliteal fossa. It swells along with joint effusions in RA & OA.

- *Lines of Blaschko* are developmental growth lines which represent the distribution of growth pads.
- *Langer's lines* are lines of minimal tension running perpendicular to the long axis of muscles.
- *No Man's land* area b/w distal palmar crease and proximal IP joint (Area of pulley's).
- *ONODI cells* are posterior ethmoidal cells which are related to optic nerve.

HALLER cells are infraorbital inferolateral extension of ethmoidal cells which are situated in the orbital floor and in the medial roof of maxillary sinus.

- *Bifurcation vertebral landmarks.*
A bifurcation occurs on 4th level of each vertebral column:
C4: bifurcation of common carotid artery
T4: bifurcation of trachea
L4: bifurcation of aorta

IMP. NEGATIVE POINTS

- Basal ganglia does NOT contain --- *Thalamus*
- Floor of the 3rd ventricle is NOT f/by --- *Oculomotor n.*
- Pupillary reflex pathway does NOT include --- *LGB*
- Not a branch of external carotid a. --- Anterior ethmoidal artery
- Not a branch of intracavernous portion of internal carotid artery --- ophthalmic artery.
- NOT seen in cavernous sinus thrombosis --- Enlarged sinus.

- NOT a content of cavernous sinus --- Optic n.
- NOT s/by anterior division of Vth n. (mandibular division) --- Medial pterygoid
- Ligament NOT present in TM joint --- Alar ligament
- NOT a pneumatic bone --- Mandible
- Prevertebral fascia is not in posterior relation to --- *Scalenus anterior*
- Vitelline vein does NOT form --- SVC
- Structure which does NOT pass through foramen magnum --- spinal cord
- Spinal cord is NOT s/b --- Throacoacromial a
- Breast is NOT s/by --- costoclavicular a
- Quadrilateral space is NOT bounded by --- *Deltoid*
- **Carpal tunnel does not contain** --- *Flexor carpi radialis tendon, palmaris longus*
- In epidural lumbar puncture structure which is NOT pierced is --- Posterior longitudinal ligament
- Utricle does NOT drain into --- Deep inguinal nodes
- Lymphatics are NOT found in --- Brain, choroid, internal ear
- Floor of femoral triangle is NOT formed by *Adductor brevis*.
- Muscles NOT attached to upper end of humerus --- long head of triceps.
- Muscles NOT inserted in 1st rib --- *Trapezius, serratus post. scalenus posterior*
- NOT a m/s of anterior compartment of leg --- *Peroneus brevis, longus* (They are m/s of lateral compartment)
(Note - *peroneus tertius* is muscle of ant. compartment of leg)
- Anal continence is NOT contributed by --- *Valves of Houston*
- Fold of GIT which are NOT permanent --- Rugae
- Artery which does NOT take part in formation of anastomosis around scapula --- *Ant. circumflex humeral a, superior thoracic artery.*
- NOT a branch of axillary artery --- *Dorsal scapular a.*
- Rotator cuff is NOT formed by --- Subscapularis.
- *Costo-sternal joint* is NOT a direct articulation of true rib
- Esophagus is NOT supplied by *Int. thoracic a* (internal mammary artery), *splenic a.*
- Structures NOT included in boundaries of Koch's Δ --- Origin of Lt. coronary artery, tendon to fossa ovalis.
- **Vein which does NOT drain (open) into the coronary sinus** --- *Anterior cardiac vein.*
- **NOT a branch of arch of aorta** --- *Rt common carotid artery, Lt brachiocephalic artery*
- Renal agenesis is NOT d/to --- failure of descent of

nephrogenetic tissue of lumbar area

- NOT a composite m/s --- Rectus femoris
- Mastoid antrum is NOT related to --- Posterior SCC.
- In post-ductal coarctation of aorta, blood vessel which does NOT form collateral --- axillary a.
- Structure which does NOT pass through esophageal hiatus --- Lt. phrenic nerve.
- Thoracic duct does NOT receive tributary from --- right bronchomediastinal lymph trunk
- Movement which does NOT take place in abduction of shoulder --- Elevation of humerus.
- Upper limb weight is NOT transmitted to axial skeleton by --- Coracoacromial ligament.
- Low radial nerve palsy does NOT include --- Sensory loss over the dorsum of hand.
- NOT true of popliteus --- Inserted at medial meniscus.
- Nerve of upper limb NOT related to humerus --- Musculocutaneous
- **Superior gluteal nerve does NOT supply --- Gluteus maximus**
- NOT a branch of splenic artery --- Right gastroepiploic artery
- NOT supplied by pelvic splanchnic nerves --- Appendix
- **Not a content of broad Ligament --- Ovary**
- Not a content of Rectus sheath --- Genitofemoral nerve
- **Hypogastric sheath is NOT formed by --- Broad ligament**
- NOT a content of adductor canal --- Femoral nerve
- NOT seen in femoral sheath --- Femoral nerve
- Femoral ring is NOT bounded by --- Femoral artery
- Urothelium does NOT line --- Membranous urethra
- NOT a content of superficial perineal pouch/space --- Sphincter urethrae
- Not a content of deep perineal pouch --- Root of penis
- NOT a sphincter of vagina --- Internal urethral sphincter
- NOT a covering of Graafian follicle --- Germinal cells
- Inguinal canal in females does NOT transmit --- Inferior epigastric artery.
- NOT a content of pudendal canal --- Nr to obturator internus
- Perineal body is NOT formed by --- Obturator internus and externus
- Structures NOT passing through greater sciatic foramen --- Obturator internus and externus
- Sacral canal does NOT contain --- L₄ - L₅ nerve roots.
- L₅ nerve root is NOT involved in --- Adduction of thigh.
- Structure NOT felt anteriorly on PR examination --- Internal iliac nodes

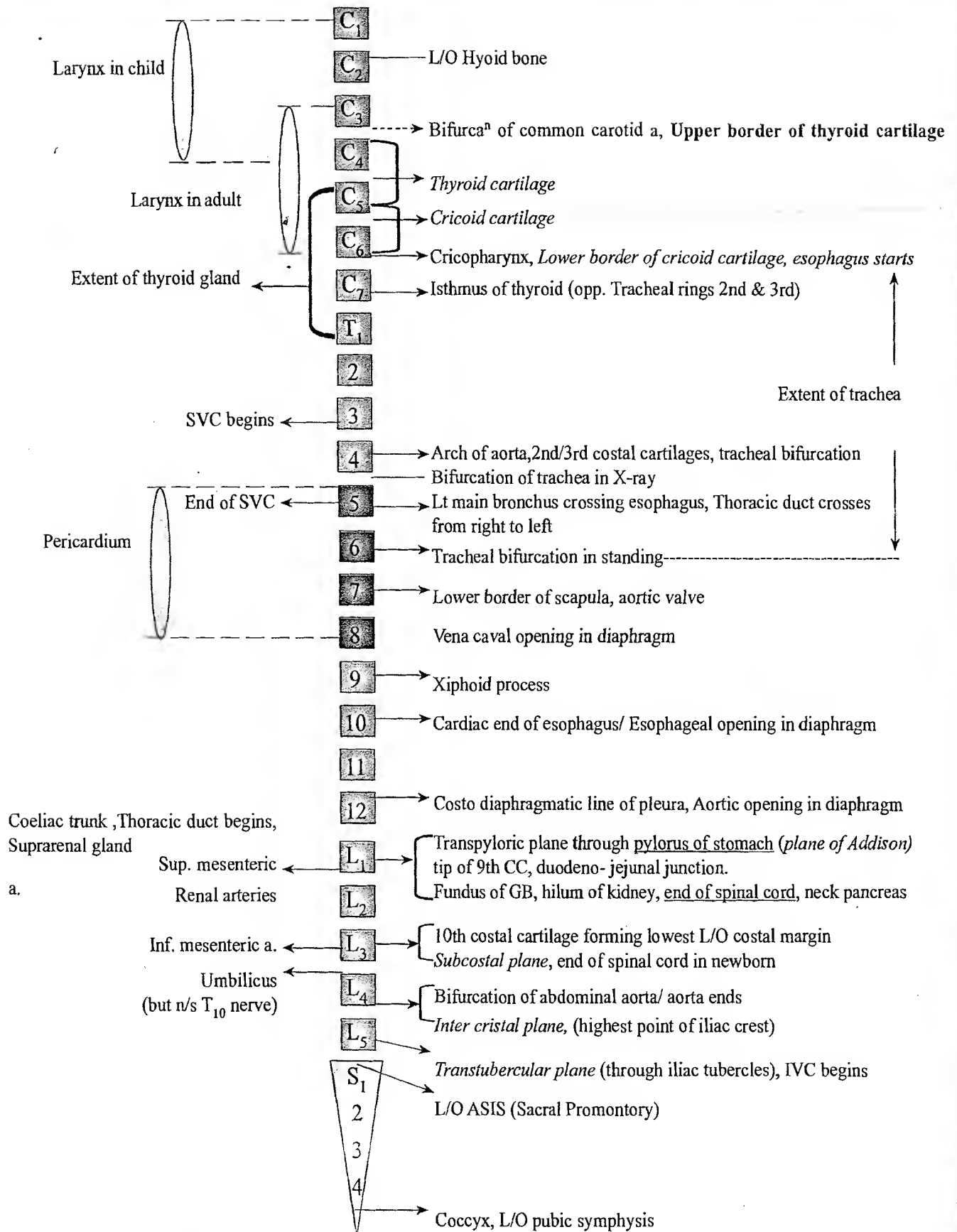
• NOT a derivative of septum transversum --- Ligamentum teres.

• NOT a derivative of pharyngeal arches --- Palatine tonsils.

• NOT a derivative of hypaxial mesoderm --- Erector spinae.

NOTES

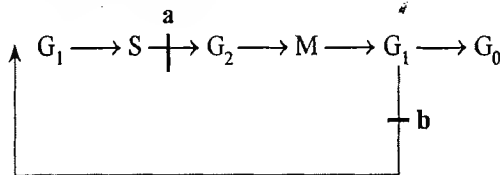
VERTEBRAL LEVELS OF IMPORTANCE



CELLULAR PHYSIOLOGY

CELL CYCLE

Block prior to G_2 phase (site a) by TGF- β will lead to \uparrow in cell size or **cell hypertrophy**



- If there is a block after M (site b), cells do not enter quiescent phase $\rightarrow \uparrow$ in cell numbers (**Cell hyperplasia**).
- Phosphorylation of RB is molecular switch (on/off) of cell cycle.
- **Cyclin D** is the 1st cyclin to \uparrow in cell cycle (first checkpoint). Appears in mid G1 but no longer detectable in S-phase. Degraded through ubiquitin proteasome pathway.
- In **M-phase** (mitosis), the rate of protein & RNA synthesis diminish abruptly while the genetic material is segregated into daughter cells.
 - Stages of Mitosis :
Prophase \rightarrow Metaphase \rightarrow Anaphase \rightarrow Telophase \rightarrow Interphase

- Spindles are formed in *late prophase* & chromosomes are attached to spindles in *metaphase*.
- In Meiosis:
 - Crossing over and chiasmata formation in *pachytene* stage of 1st meiotic division.
 - Genetic shuffling occurs in *second meiotic division*.

- $\rightarrow G_2$ -M phase cells are most susceptible to radiation injury.
- \rightarrow Barr body is found in interphase of cell cycle.
- \rightarrow Cell cycle regulators in cell growth are cyclins & kinases.
- \rightarrow Mitotic spindles are formed by microtubules which contain tubulins.
- \rightarrow Vincristine and vinblastine act by breaking microtubules, while paclitaxel stabilizes them. Colchicine is also a mitotic inhibitor

Radiation injury to the cell

- If cells are irradiated in G_1 phase, chromosomal aberrations may occur.
- If cells are irradiated in G_2 phase, chromatid aberration may occur.
- Cells are most radiosensitive in **G_2 -M interface** and most resistant towards the end of S-phase ($M > G_2 > G_1 > S$).

	G_1	S	G_2	M	G_0
<i>K/as</i>	Pre-synthetic phase (Gap 1 or interphase)	Synthetic	Post-synthetic	Mitotic	Quiescent
<i>Characteristics</i>	Most variable phase replication occurs [Cellular content of DNA doubles]	Chromosomal/ DNA	Cell cycle arrest d/t p 53	Rate of protein and RNA synthesis \downarrow es abruptly	Gene transcription
<i>Events</i>	Max ^m part of cell cycle	DNA synthesis	RNA synthesis		
<i>Importance</i>	1. Growth factors are most effective 2. First checkpoint in cancer	In malignant cells there is \uparrow nuclear cytoplasmic ratio			Non-proliferating cells remain in G_0 (Quiescent) stage in this phase.
<i>Blocked by</i>	Vinblastine	Mtx, doxo, cytarabine, 6-TG, hydroxyurea, mitomycin-C, 6-MP	Bleomycin, etopo dauno-, topotecan	Vincristine/blastine paclitaxel, colchicine	
<i>Effect of irradiation</i>	Chromosomal abnormalities	Chromatid aberration		Most radiosensitive at G_2 -M interface	

EXTRACELLULAR MATRIX (ECM)

- Cells are surrounded by extracellular matrix often referred to as connective tissue.
- ECM contains 3 major classes of molecules
 1. Structural fibrous proteins — Collagen, Elastin, Fibrillin
 2. Adhesive glycoproteins --- Fibronectin, Laminin
 3. Glycans — Hyluronic acid, Sulfates (chondroitin, keratan, heparan, dermatan)

Collagen

Collagen is the **most abundant** protein found in animal world. It constitutes ~ 25% of the mammalian proteins. It has triple helix structure.

Elastin

Provides extensibility and recoil on lung, blood vessels, and ligaments.

Fibrillin

Fibrillin is a large glycoprotein present in microfibrils (in the zonular fibres of lens, periosteum, elastin fibres of aorta). Mutations in **fibrillin-1** gene result in **Marfan's syndrome** while mutations in fibrillin-2 result in congenital contractural arachnodactyly.

Fibronectin

Important glycoprotein involved in cell adhesion & migration. Fibronectin receptor interact indirectly with actin microfilaments present in cytosol.

Integrin (cell adhesion molecules)

Part of cell membrane that mediates cellular attachment to ECM

Sarcolemmal proteins

Proteins/ glycoproteins related to sarcolemma are of two types.

Transmembrane proteins	Dystroglycans, sarcoglycans, caveolin-3, integrins
Proteins localised to cytoplasmic face of membrane	Dystrophin, dysferlin, calpain

- *Perlecan is a large multidomain proteoglycan found in ECM.*
- *Glycosaminoglycans (found in proteoglycans) are built up of repeating disaccharides*
- *Defect in sarcolemmal proteins and glycoproteins and their complexes results in selected muscular dystrophies.*
- *Laminin is the most abundant glycoprotein present in basal lamina and glomerular basement membrane (GBM). Laminins are cross-shaped molecules which bind to CAM*

Cell adhesion molecules (CAMs)

- Integrins
- Cadherins
- Selectins
- IgG superfamily molecules

Molecular motors

Microtubular based

- Kinesin
- Dyneins

Actin based

- Myosin I-V

Cytoskeleton of a cell

- Cytoskeleton of a cell is formed by
 1. **Microfilaments** (made up of actin and myosin),
 2. **Microtubules** (made up of tubulin proteins)
 3. **Intermediate filaments** IF resist external pressure but are not involved in movement of cell/flagella
- Motility of a cell is d/to tubulin proteins present in microtubules. Microtubules are essential for leucocyte migration and phagocytosis
- Coordinated **dynein-microtubule interactions** within the axoneme are the basis of ciliary and sperm movement.

→ *Microtubules associated proteins are : Kinesin, dynein, and dynamin*

→ *Centrosome is the organizing centre of cell for assembly of microtubules*

→ *Actin is the most abundant protein present in mammalian cells*

→ *Selectins play key roles in inflammation and in lymphocyte homing*

Intercellular connections

- Tight junctions (zona occludens) tie cells together. They provide strength and stability to cells. The desmosomes and zona adherens also help to hold cell together.
- Transmembrane proteins that form tight junctions are ---

occludins, JAMs, claudins

- Hemidesmosomes and focal adhesions attach cells to their basal laminas.

Exocytosis Vs. Endocytosis

Properties	Exocytosis	Endocytosis
• Definition	Extrusion of proteins from Golgi apparatus	Reverse of exocytosis
• Examples	Phagocytosis (cell eating), Pinocytosis (cell drinking), Emeioctosis (reverse pinocytosis) is a type of exocytosis responsible for insulin secretion. Promoted by Ca^{++} , K^{+} Inhibited by Mg^{++}	Receptor mediated endocytosis via - <i>Clathrin</i> by endosomes for LDL digestion - <i>Caveolin</i> mediates cellular ingestion of various vitamins - <i>Dyanamin</i> (a GTP binding protein)
• Require	Ca^{++} dependent process. Also require energy	Energy

- *Clathrin mediates receptor-mediated endocytosis of ligands, e.g. LDL lipoprotein, NGF, transferrin, growth factors, antibodies and many others.*
- *Caveoli are abundant in smooth muscle, type I pneumocytes, fibroblasts, adipocytes, and endothelial cells.*

CELL ORGANELLES

Endoplasmic Reticulum

Two types--

Granular/ Rough ER

- Contain ribosomes or granules attached to cytoplasmic side of the membrane
- Synthesize secretory proteins, cell membrane proteins and lysosomal enzymes
- Site of co-translational modifications of proteins, initial folding of polypeptide chain proteins into 3D structure (i.e. they are site of protein synthesis)

Agranular/ Smooth ER

- Does not contain ribosomes
- Synthesize lipids (steroid hormones, membrane phospholipid & cholesterol)
- Site of fatty acid elongation, drug detoxification. Provides enzymes that control glycogen breakdown

Golgi apparatus

- Also k/as dictyosome
- Site of **post translational modification** of proteins such as glycosylation.
- Involved in processing, packaging and **sorting** of proteins (Secretory protein like insulin is packaged into clathrin coated vesicles)

Ribosomes

- Are granules composed of protein and rRNA
- **Polysomes** (polyribosomes) are formed by ribosomes + mRNA, involved in synthesis of cytoplasmic proteins
- Site of **translation** (of mRNA into a/a sequence)
- Free ribosomes are found in cytoplasm. They synthesize cytoplasmic proteins e.g. hemoglobin

Mitochondria

- Synthesize ATP and k/as " Powerhouse / energy house of cell "
- Site of Krebs's cycle, β - oxidation of FA, oxidative phosphorylation, acetyl CoA production
- Both imports and synthesize proteins
- Matrix contains mitochondrial DNA, mRNA, tRNA and rRNA
- **Mitochondrial DNA:** It is a double stranded circular molecule. Inheritance of mitochondrial DNA is strictly **maternal**. Mutation of it results in Leber's hereditary atrophy.

Lysosomes

- Interior is more acidic d/to action of a proton pump (H^{+} ATPase)
- Contain **lytic enzymes** e.g. ribonuclease, deoxyribonuclease, phosphatase, glycosidase, arylsulfatases, collagenase, cathepsins
- Vitamin A overdose causes injury to lysosomes.

Organelle	Function
• Nucleolus	Site of synthesis of r-RNA
• Ribosomes	Site of protein synthesis, translation of mRNA
• RER/ Granular ER	Site of protein synthesis (e.g. hormones, proteins found in enzymes)

• SER/ Agranular ER	Site of steroid synthesis / detoxification/ FA elongation
• Golgi Body	Processing/ packaging, intracellular sorting of proteins , formation of lysosomes
• Lysosomes	Contain digestive/ lytic enzymes and hydrolases (suicidal bags of cell)
• Peroxisomes	Contain oxidases

- Largest organelle of eukaryotic cell is — ER
- Sarcoplasmic reticulum is modified ER found in skeletal and cardiac m/s.
- Proteins synthesized and sorted in RER include proteins destined for membranes (e.g. ER, Golgi, lysosomal, and plasma membrane) and proteins destined for secretion (i.e. secretory proteins)
- Nissle's granules/bodies are granular material located in the intracytoplasmic ribosomes of neurons. Stains intensively with basic dyes. In EM these bodies are seen composed of RER & contains Ribonucleoproteins.
- Lipofuscin/lipochrome is a wear & tear pigment. Yellow-brown intracellular lipid pigment found in atrophied cells in old age (brown atrophy of heart, senile dementia (deposition in neurons) & in severe wasting d/ to malnutrition. C/b stained by fat stains, fluorescent and acid fast stains.
- Döhle bodies are light blue-gray, oval, basophilic, leukocyte inclusions located in the peripheral cytoplasm of neutrophils. Consist of ribosomes and endoplasmic reticulum. Found in bacterial infections and in a benign inherited condition k/as May-Heggling Anomaly.
- Barr body is the condensed, single X-chromosome, (heterochromatinized X-chromosomes). Appears as a densely staining mass in the nuclei of somatic cells of female mammals in interphase of cell cycle.
- Sex chromatin is a small condensed mass of the inactivated X-chromosome usually located just inside the nuclear membrane of the interphase nucleus; the number of sex chromatin bodies per nucleus is one less than the number of X-chromosomes; normal males and females with Turner syndrome (XO) have none (sex chromatin negative), normal females and males with Klinefelter syndrome (XXY) have one, and XXX-females have two.

ESR and BMR

ESR is ↓ in	BMR is ↑ in	BMR is ↓ in
• Polycythemia vera	• Exercise, fever	• Obesity
• Smoking	• Feeding	• Starvation (↓ in lean body mass)
• CHF	• Hyperthyroidism	• Hypothyroidism,
• Sickle cell disease	• ↑ air m/s mass, ↑ 2,3 DPG	• Old age

- Energy expenditure in resting state is almost equal to BMR.
- BMR depends upon lean body mass

Newtonian Fluid

- Velocity is constant. Velocity does not change with change in shearing force (e.g. - Water)
- When N~ fluid moves through a tube shows *laminar* (streamline flow)

Non-Newtonian fluid

- Shows an anomalous viscosity, that is, with change of shearing force, the viscosity also changes (e.g. - Blood)
Viscosity increases with change in velocity.

Membrane fluidity

- Fluidity of membrane is highly dependent upon the lipid composition of the membrane.
- Membrane lipids are amphipathic and form bilayer.
- Fluidity is ↑ by --- ↑ temperature, ↑ in double bonds, e.g. Unsaturated FA.
- Fluidity is ↓ by --- Saturated FA e.g. stearic acid and palmitic acid.
- Cholesterol ↓ membrane fluidity at moderate temperatures by reducing phospholipid movement, But at low temperatures it hinders solidification by disrupting the regular packing of phospholipids. Cholesterol is known as "temperature buffer".
- As membrane fluidity increases so its permeability to water and other small hydrophilic molecules.

Green House Effect/Global Warming

- It is because of emission of green house gases (CO₂ most common, Ozone, chloro- fluorocarbons, Halons, Methane & N₂O) into the atmosphere.
- Responsible for increase in average global surface temperature.
- NOT seen with N₂.
- Stratosphere of ozone protects from harmful UV rays.

Transport across biomembrane

Mechanism	Mode of transport	Kinetic	Examples
Active Transport	Carrier mediated	Against concentration & electrical (electro-chemical) gradient, energy (ATP) required	Na ⁺ K ⁺ ATPase (sodium pump)
Facilitated diffusion	Passive from high → low energy, But carrier is reqd.	Substance is moved in the direction of electro-chemical gradient	Glucose transporters (GLUTs), Hormones
Simple diffusion	Passive, Carrier is NOT required		Diffusion of lipid soluble drugs
Osmosis	Passive	Fluid shifts from hypo → hyperosmolar compartment	

→ Ionophores are transmembrane proteins that control transport of ions (small organic molecules) across the biological membrane

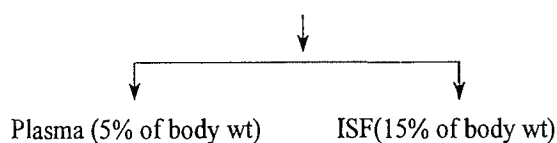
→ Extracellular ligands are called first messenger while intracellular mediators are second messengers.

Distribution of body water

• Body is composed of 60% of water and 40% of organic/inorganic material (18% protein + 15% fat + 7% minerals).

• Of this body water ICF is 2/3rd and ECF is 1/3rd.

ICF	ECF
66% of body water	33% of body water
(40% of body weight)	(20% of body wt)



• Total blood volume is 8% of body weight (roughly 5 kg in a 60 kg man) or it is 65 ml/kg

• Values in a 60 kg man

60kg	→	36	→	24	→	12	→	9	→	3
(Total body wt)		(Water)		(ICF)		(ECF)		(ISF)		(Plasma)

Measurement of

Measurement of	By
• TBW (Total body water)	D ₂ O (Deuterium oxide/ heavy water), Tritium oxide, aminopyrine
• ECF	Inulin (most accurate), mannitol, sucrose
• Plasma volume	Evans blue, s. albumin labelled iodine
• Red cell volume	Tagged RBCs
• Total blood volume	= Plasma volume × $\frac{100}{100 - Hct}$
• ISF (Interstitial fluid)	ISF = ECF - Plasma volume
• ICF (Intracellular fluid)	ICF = TBW (Total body fluid) - ECF

Distribution of ions in body (concⁿ in mmol/L)

ICF					
cations			anions		
K ⁺	>	Na ⁺	>	H ⁺	A ⁻
↓		↓		↓	↓
155		12		0.00013	155
					>HCO ₃ ⁻
					↓
					8
					Cl ⁻
					↓
					3.8

ECF				
cations			anions	
Na ⁺	>	K ⁺	>	H ⁺
↓		↓		↓
145		4		0.000038
				Cl ⁻
				↓
				120
				HCO ₃ ⁻
				↓
				27

A⁻ = Organic Anions

Permeability across lipid bilayer membrane

H ₂ O	>	Indole	>	Urea	>	Glycerol
Co-efficient		(10 ⁻²)		(10 ⁻⁴)		(10 ⁻⁶)

Tryptophan	>	Glucose	>	Cl ⁻	>	K ⁺	>	Na ⁺
				↓				(10 ⁻¹²)
				Most diffusible ion				Least diffusible ion

- So in ICF major cation is K^+ & anions are organic anions ($PO_4 > Pr^-$)
- In ECF major cation is Na^+ and major anion is Cl^-
- 91% of total body sodium is extracellular, of this maximum (36.5%) is in bone.
- Water is freely permeable & urea is most diffusible substance.
- In resting tissue (as well as in excitable tissue) easily/most diffusible ion is Cl^- and least/non diffusible ion is Na^+ .
- The bicarbonate buffer system is the primary buffer system for the ECF. The phosphate buffer system does not have a role in regulating ECF pH, but it is a very effective buffer system in urine and the intracellular fluid (ICF).⁴
- Proteins are the most abundant buffers in the body. At least 3/4th of the body's buffering capacity is via intracellular proteins. Hemoglobin is an important protein buffer.
- Most abundant buffer in plasma or in ICF is → Proteins

Most Abundant Ions Chart

Properties	Cation	Anion	Ion
Most abundant extracellular	Na^+	Cl^-	Cl^-
Most abundant intracellular	$K^+ > Mg^{++}$	PO_4	Organic anions

BUFFERS IN THE BODY

- Extracellular buffers include bicarbonate and ammonia, whereas proteins and phosphate act as intracellular buffers.
- Bicarbonate is the most important, most abundant and primary buffer in the extracellular fluid & in plasma. The alkaline reserve refers to the available bicarbonate buffering capacity.
- Proteins may be considered the **most abundant** buffer in the intracellular fluid /ICF (& in body as well). Haemoglobin is an example of protein buffer & is more important buffer than plasma proteins.
- The protein buffer system is an abundant and powerful means of regulating pH inside cells, and has a limited role in buffering the blood plasma.
- The phosphate buffer system does not have a role in regulating ECF pH, but it is a very effective buffer system in urine and the intracellular fluid (ICF).
- Physiological regulators of blood pH include the respiratory and renal systems. The rate and depth of respiration are

affected by changes in CO_2 levels.

- Addition of a strong acid to the extracellular fluid would result in the \uparrow formation of H_2CO_3 .
- The primary determinant of body fluid volume is the number of sodium and chloride ions lost from the kidney.
- The m/c cause of acid-base imbalance is respiratory acidosis, a result of elevated blood levels of CO_2 due to shallow breathing, suffocation, or lung diseases that impede O_2 and CO_2 exchange.
- Hyperventilation leads to the levels of CO_2 to drop to below normal levels and can cause **respiratory alkalosis**.

PLASMA

- **Osmolarity** is number of osmoles per litre of solution. It changes with temperature & pressure of other solutes.
- **Osmolality** is number of osmoles per kg of solvent. It does not change with temperature, so preferred.
- **Tonicity** is osmolality of a solution relative to plasma. 0.9% NaCl and 5% dextrose are isotonic to plasma. Distilled water is hypotonic while 20% mannitol is hypertonic to plasma.

$$\text{Osmolality (mosm/L)} = 2[Na^+]_{\text{meq/L}} + 0.55[\text{Glucose}]_{\text{mg\%}} + 0.36[\text{Urea}]_{\text{mg\%}}$$

In state of osmotic equilibrium, osmolality of ECF = ICF

- Osmolality of plasma is 280 - 290 mosm/L.
- Contribution to plasma osmolality is maximum of Na^+ and its associated anions which is ~ 270 mosm/L. Plasma osmolality is roughly $2 \times [Na^+]$.
- Contribution to osmolality of plasma
 - Na^+ and its associated anions which is ~ 270 mosm/L
 - Glucose 5 mosm/L
 - Urea 5 mosm/L
 - Proteins 2 mosm/L
 - K^+ is intracellular, so hardly any effect
- Colloidal osmotic pressure of plasma is also k/a oncotic pressure & it is mainly d/to plasma proteins esp albumin.

- All buffer pairs in a homogenous solution are in equilibrium with the same $[H^+]$ — **Isohydric principle**.
- When acids are placed into solution $pH = pK_a + \log \frac{[A^-]}{[HA]}$ — **Henderson Hasselbach equation**
- Ficks law or Fick's principle deals with diffusion

- In presence of a non-diffusible ion, the diffusible ion distribute themselves so that at equilibrium their concentration ratios are equal **Gibbs Donnan effect**.
- At equilibrium the distribution of permanent ions across the membrane is assymetric and an electric gradient exists, whose magnitude c/b determined by **Nernst equation**.
- Cell membrane is semi-permeable. Maximum permeability is of $K^+ \gg Cl^- > Na^+$. Contribution of Na^+ to RMP is negligible.

Plasma Proteins

- There are 3 major plasma proteins--- Albumin, globulin and fibrinogen.
- Most of the plasma proteins are synthesized in liver but antibodies (γ -globulins) are synthesized from lymphocytes.
- Oncotic pressure of plasma is mainly d/to --- albumin
- Albumin : Globulin ratio = 2:1 which is 3.6-5.2 gm% : 1.7-3.9 gm% (varies b/w 1.5:1 or 1.2:1)
- Anti proteases plasma proteins are --- anti-chymotrypsin, α_1 - chymotrypsin, α_2 - Macroglobulin, antithrombin

1. Albumin

Most abundant plasma protein, exerts 70-80% (maximum) of colloidal osmotic or oncotic pressure. Albumin is capable of bind and transports FFA, unconjugated bilirubin, Ca^{++} , steroid hm, T_3 , copper. It has low viscosity (**LMW, high concentration in blood**). Drugs like sulfonamides, pen G, dicumarol, and aspirin are bound to albumin.

2. Globulins

Types	Examples	Function
α_1	α_1 -acid glycoprotein (orosomucoid)	Binds progesterone
	AFP (α_1 -fetoprotein)	
	α_1 AT(Antitrypsin/ Anti-proteinase)	
	Trypsin, plasmin, thrombin	
α_2	1. Ceruloplasmin	Binds & transport copper ion (Cu^{++}) in plasma. Ferro-oxidase activity
	2. Haptoglobin	Binds extra-corpuseular Hb, Peroxidase activity
	3. Hemopexin	Binds heme

α	1. β -Lipoproteins (LDL)	
	2. Transferrin (Siderophyllin)	Bacteriostatic, Fe carrier
	3. CRP	

- Antibodies are γ -globulin
- β_2 microglobulin levels are \uparrow in patients on chronic dialysis (hemodialysis related amyloidosis)
- Serum β_2 microglobulin is the single most powerful predictor of survival (prognostic indicator) in patients with Multiple myeloma.
- α_2 macroglobulin is a large plasma glycoprotein which has a role in transport of zinc and acts as a pan-proteinases inhibitor.

3. Fibrinogen

- Large size molecule, contributes **viscosity** of blood

Transport or binding proteins in plasma

- Ceruloplasmin — Binds & transport copper ion (Cu^{++}) in plasma
- Transferrin — Transports iron
- Ferritin — Storage form of iron in tissues
- Transthyretin — Binds & transports thyroxine (TBG) & retinol (Prealbumin)
- Transcortin — Binds cortisol(cortisol binding globulin; CBG)
- Haptoglobin — Binds extracorpuseular Hb (levels are \downarrow in hemolytic anemias)
- Hemopexin — Binds heme

Acute Phase Proteins

The level of certain plasma proteins is \uparrow ed during acute inflammation or secondary to tissue damage. These proteins are k/as "acute phase proteins or reactants". E.g.

- CRP
- Haptoglobin
- α_1 antitrypsin, α_1 acid glycoprotein
- Procalcitonin (Specific marker in neonatal sepsis)

NFkB (Nuclear factor kappa -B) is a transcription factor that stimulates the synthesis of acute phase reactants. Molecules which stimulate synthesis of acute phase reactants are --- IL-1 mainly, IL-6 also.

CRP (C-reactive protein)

- CRP is a β - globulin. CRP, so called because it reacts with C polysaccharide of pneumococci

- *C-substance* is produced by pneumococci which is precipitated by CRP, that appears in acute phase sera of patients suffering from pneumonia or septicemia.
- Thus CRP is a marker / sensitive indicator of infection, inflammation, tissue injury, CVS conditions secondary to atherosclerosis and solid tumours
- It can bind heme, T-cells and can activate complement.

NERVE FIBRES

● RMP (Resting membrane potential)

RMP or resting voltage is mainly d/to K^+ ions (transport through K^+ channels) and an ion pump called the Na^+/K^+ -ATPase. In all excitable tissues (including heart m/s) RMP is affected by changes in ECF K^+ concentration. \uparrow se in K^+ causes \downarrow se RMP of cell.

● AP (Action potential)

In neurons AP originates at the **axon hillock**. AP is d/ to Na^+ influx. Magnitude of AP is affected by ECF Na^+ \downarrow ing the ECF Na^+ concentration \downarrow es the size of AP but has little effect on RMP.

AP is comprised of the following stages:

1. **Resting Stage:** It is the polarized stage of the membrane. The RMP present in this stage is $-90mV$.
2. **Depolarization:** Membrane suddenly becomes very permeable to Na^+ ions. The initially present polarized state is neutralized by inflow of Na^+ ions. Then, the MP rises rapidly in +ve direction ($-90mV$ to $-70mV$, $-50mV$ to $0mV$ and finally to $+30mV$).
3. **Repolarization:** It is c/by K^+ efflux which re-establishes normal RMP. The diffusion of K^+ ions takes place d/to opening of K^+ channels.
4. **Hyperpolarization:** MP becomes more negative than the RMP. The nerve at this stage is said to be hyperpolarized. Hyperpolarization (from -70 to -90 mv) is d/to $\uparrow K^+$

- **Hypocalcemia** \uparrow es the hyper-excitability of nerve fibres & muscles cells by \downarrow ing the amount of depolarization necessary to initiate the changes in Na^+ & K^+ conductance that produces the AP (conversely hypercalcemia stabilizes the membrane by \downarrow ing excitability. Hypercalcemia may precipitate cardiac arrest).

- Cl^- ion is the most diffusible & Na^+ is least / non diffusible ion both in resting as well as in excitable tissue

- Chemical gradient across the cell membrane is maintained chiefly by K^+

Nerve Fibres Erlanger & Gasser's

classification

Fibre	Type	Subtype	Numerical classification of sensory neurons	Origin	Function	Diameter μm	Conduction Velocity
Myelinated	A	$A\alpha$	Ia	M/s spindle, annulospiral end (Ia), Golgi tendon organ (Ib)	Proprioception, somatic motor	15-20 (Max ^m)	70-120 (Max ^m)
			Ib				
		$A\beta$	II	M/s spindle, flower spray ending, touch, pressure receptors	Touch, pressure	5-12	30-70
		$A\gamma$			Motor to m/s spindles	3-6	15-30
		$A\delta$	III	Pain & cold some touch receptors	Fast pain, cold, touch	2-5	3-15
Partially myelinated	B				Preganglionic autonomic efferents	<3	3-15
Non-myelinated	C	Dorsal root	IV	Pain, temperature & other receptors	Slow pain, temp. (cold/warmth), some mechanoreceptor reflex response	0.4-1.2	0.3-2
		Sympathetic			Post ganglionic sympathetic	0.3-1.3	0.7-2.3

• Susceptibility of nerve fibres to

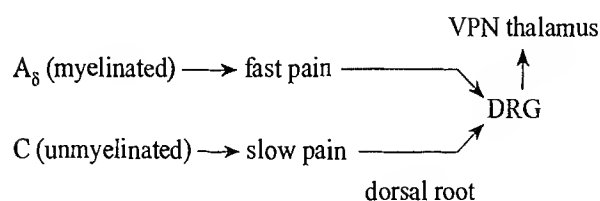
1. Pressure $A > B > C$
2. Hypoxia $B > A > C$
3. Local anaesthetic/Cocaine $C > A > B$

[Remember PHC/ABC]

- Sensory axons are Ia($A\alpha$), Ib($A\alpha$), II($A\beta$), III($A\delta$) & IV (C)
- Motor axons are Alpha ($A\alpha$), Gamma ($A\gamma$), B & C
- Fast pain is carried by $A\delta$ and slow pain by C fibres
- Afferent for cold are $A\delta$ and C fibres whereas afferents for warmth are C fibres.
- A type fibres are myelinated and C fibres are non-myelinated. B fibres have some myelination.

Pain pathway

Sense organs for pain are free nerve ending found in almost every tissue of the body



- Substance P is mediator of pain.
- Afferent limb of autonomic/visceral nervous system carries sensory information (pain) by sympathetic unmyelinated C fibres. Relief mechanism of massage and counterirritants
- Hot water bag used for abdominal pain works by stimulation of $A\delta$ fibres thus inhibiting adrenergic receptors.

Nerve Conduction

- Nerve impulse (axon potential) begins in the segment of axon k/as **axon hillock**. It has lowest threshold potential d/to high no. of Na^+ channels/unit area.
- Highest concentration of Na^+ channels/unit area is seen in node of Ranvier.
- AP in **motor** neurons arises from axon hillock.
- AP in **sensory** neurons arises from initial node of Ranvier.
- Sensory neurons are DRG cells (pseudounipolar cells).
- Conduction is faster in myelinated axons.
- Synapses generally permit conduction of impulses in direction only because neurotransmitter substance is present in vesicles of presynaptic neurons only.

Weber Feschner's Law.

It is a law for intensity discrimination. It provides relationship b/w the intensity of stimulus, the size of generator potential and frequency of AP.

Magnitude of stimulus perceived \propto log of intensity of stimulus strength
[Size of sensation felt]

Power law describes interpreted signal strength. ($R = KS^ay$).
Law of intensity discrimination

As the intensity of a stimulus is increased, it spreads over a large area and activates more and more receptors, called recruitment of sensory units.

Bell Megendie Law

Dorsal roots are sensory & ventral (anterior) roots are motor.

Law of Projection

Phantom limb phenomena

Law of specific nerve energies (Muller's Doctrine)

When the nerve path from a particular sense organ is stimulated, the sensation evoked is that for which the receptor is specialized no matter how or where along the pathway the activity is generated.

MUSCLE FIBRES

Muscle Proteins / Myofibrillar proteins

3 types

1. Protein of thick myofilament is --- Myosin
2. Proteins of thin myofilaments are --- Actin, tropomyosin, and troponin.
3. Scaffold proteins --- Actinin, titin, desmin, dystrophin

Myosin

- Major protein of m/s, constitutes 60% of m/s proteins. The type present in muscles is myosin II
- Actin binding protein. Length is 71 nm.

Actin

- F-actin has an active site that interacts with myosin

Tropomyosin

- It covers the actin binding sites of myosin heads.: remember

with the funda that tropomyosin is on the top of myosin. It blocks the active site F-actin during relaxation (i.e. blocks interaction of actin and myosin in skeletal muscles)

Troponin

- Present in skeletal and cardiac muscles (but not in smooth m/s). Has 3 subunits.

Troponin T	Troponin I	Troponin C
Binds to tropomyosin	Inhibitory. Inhibits myosin - actin interaction	Binds calcium. It brings <u>contraction</u> by removing effect of tropomyosin

Titin (connectin)

- Is the largest protein molecule yet described.
- It connects Z line to M lines (so also called **connectin**) & provides scaffolding for the sarcomere.
- It is an extra ordinarily long, flexible and slender myofibrillar protein, provides elasticity to the heart.

Desmin

- M/s specific intermediate filament protein

Phospholamban

- Regulates the activity of Ca^{++} pump on sarcoplasmic reticulum (inhibits SR-calcium pump)
- Its inactivation \uparrow ses Ca^{++} sequestration by SR which leads to
 - \downarrow duration of contraction in cardiac m/s
 - Relaxation in smooth m/s
 - Little/no effect on skeletal m/s

Calmodulin

- Activated by binding of Ca^{++} in SM (Interacellular Ca^{++} binding proteins)
- It activates MLCK \rightarrow smooth m/s contraction. It activate phosphorylase kinase \rightarrow phosphorylase, also calcineurin (inactivates Ca^{++} channel by dephosphorylating them). It also activates T- cells & is stimulated by immunosuppressants.

- \rightarrow Intracellular Ca^{++} is required for contraction in all 3 types of m/s i.e. skeletal, smooth and cardiac muscles
- \rightarrow Excitation contraction coupling in SM requires —Binding of Ca^{++} with calmodulin
- \rightarrow Excitation contraction coupling in cardiac/ skeletal m/s requires —Binding of Ca^{++} with troponin C
- \rightarrow Sustained contraction (as in smooth m/s) is d/to —Latch bridge mechanism

- \rightarrow **Sarcomere** : Is the basic unit of contraction and it is the distance b/w two adjacent Z- discs. In each sarcomere I- bands become narrower during m/s contraction
- \rightarrow **Rheobase** : Minimum strength of current (stimulus) to produce a response.
- \rightarrow **Utilisation time** : Time taken by a rheobase current to produce a response.
- \rightarrow **Chronaxie** : Time taken by twice of rheobase current to produce a response. Chronaxie of a nerve is less than that of m/s.

Treppe or staircase phenomena

When a series of maximal stimuli is delivered to skeletal m/s at sub-tetanzing frequency, tension raises during each twich. After several contractions a uniform tension per contraction is reached. This phenomena is k/as T~

Skeletal, Smooth & Cardiac Muscles

Properties	Skeletal m/s	Smooth m/s	Cardiac
Actin, myosin, tropomyosin	+	+	
Troponin	+	—	
Contraction	Phasic	Tonic, sustained	
Chronaxie	longer	Shorter	
EPP	+	—	
Automaticity, Rhythmicity	—nt	+	+
Cross striations	—	+	+
Nucleus	Single, central	Multiple (multinucleate), peripheral	Single, central
Syncytium	+	—	+
Intercalated disc	—	—	+
Syncytium	+	—	+
RMP is	—90 mV	—50 mV	

Muscle Contraction

Excitation contraction coupling

- Ca^{++} is excitation-contraction coupling agent.
- Ca^{++} from sarcoplasmic reticulum
 - \downarrow
 - Combines with Trop-C
 - \downarrow
 - Tropomyosin leaves the actin-myosin site
 - \downarrow
 - Contraction

Relaxation

- Ca⁺⁺ is pumped back into SR with the help of SERCA (Sarcoplasmic endoplasmic reticulum, Ca⁺⁺ pump).
- Activity of SERCA is inhibited by phospholamban.

Isometric contraction

When contraction occurs without an appreciable \uparrow in m/s length of whole muscle. isometric: force = effort (no movement)
isokinetic: speed and tension remain constant through ROM (special machines)

Isotonic contraction

Contraction occurs against a constant load. Isotonic contraction do work in body building. Tension constant - speed differs (most weights exercises are isotonic)

In cardiac m/s

- β stimulation \uparrow cAMP



Inhibits the phospholamban by phosphorylation



\uparrow SERCA activity

- Absolute refractory period (ARP) in cardiac m/s**
Lasts till cardiac contraction lasts (Includes phase 0, 1, 2 & half of 3). Corresponds with duration of AP and it is longer than ARP in skeletal muscles. No AP from another part of heart will re-excite the m/s when heart muscle is in ARP.

Pacemaker cells

Pacemaker potential (RMP is -50 to -60 mV). In pacemaker cells depolarisation is d/to Ca⁺⁺ influx.

Prepotential

D/to K⁺ efflux (spontaneous depolarisation), opening of h/f (hyperpolarisation/funny) channels & opening of Ca⁺⁺ T-channels.

In Smooth m/s

- RMP is -50 to -60 mV. It is not a straight line but is undulating & wavy k/as BER (Basal Electrical Rythm).
- It is spike potential (not the BER) which produces contractions in SM. Depolarisation is d/to Ca⁺⁺ influx while repolarisation is d/to K⁺ efflux.
- BER is d/to oscillations in activity of Na/K pump. These 5 to 15 mV oscillations vary in different part of GIT. Max^m frequency is seen in duodenum (12/min) while mini^m in sigmoid colon (3/min)

Extract:

In	RMP (mV)	AP (mV)	Depolarisation is d/to	Repolarisation is d/to
Nerve fibre	-90	+30	Na ⁺ influx	K ⁺ efflux
Skeletal m/s	-90		Na ⁺ influx	K ⁺ efflux
Smooth m/s	-50 to -60		Ca ⁺⁺ influx	K ⁺ efflux
Cardiac m/s: ventricular	-90		Na ⁺ influx	Na ⁺ efflux (initial), K ⁺ efflux (final)
Cardiac pacemaker cells	-55		Ca ⁺⁺ influx	-

End Plate Potential (EPP)

It is a depolarization potential. It develops at N_M junction in skeletal and cardiac muscles but not in SM.

	EPP	AP
1. Type	local event; Confined to motor end plate	-
2. Propagate	No	Yes
3. Decrement with time	Yes	No
4. All or none phenomena	-	+
5. Stronger stimulus causes	EPP of more value, Forerunner of AP	

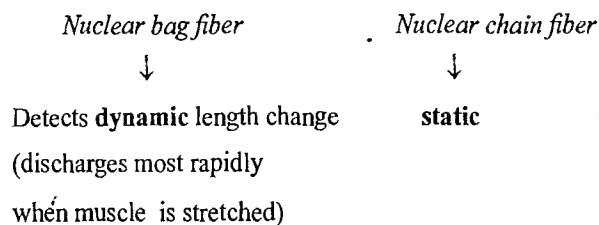
- For development of AP an adequate stimulus is enough. Stimulus which is stronger than adequate do not produce bigger APs (**all or none phenomena**)

- Equilibrium potential for an ion (e.g. Na⁺) is calculated by Nernst equation
- CRO (Cathode ray oscilloscope) is used to record electrical events (EPP) in a mammalian tissue.
- Synaptic potential is recorded by— micro electrodes.
- EPP at N_M junction (like EPSP at synapse) belongs to the class of **graded potential**. Greater the stimulus greater is the intensity of EPP.
- EPSP is d/to opening of Na⁺ & Ca⁺⁺ channels (mainly influx of Na⁺ channels)
- IPSP is d/to influx or opening of Cl⁻ & K⁺ channels (or closure of Na⁺ & Ca⁺⁺ channels)

Muscle Spindle

- It activates myotactic/ **stretch reflex** that operates to maintain muscle length. M~ have 2 types of fibres:
 1. *Extrafusar* — innervated by α -motor neuron

2. *Intrafusal* — innervated by γ -motor neuron. Further intrafusal fibers are of 2 types.



Golgi tendon organs

- They activate **inverse stretch reflex** (inverse myotactic reflex).
- Transmit sensory information via group **Ib** afferents.
- They respond to the degree of **muscle tension** (or force generated in m/s during contraction).

- Each Golgi tendon organ consists of a capsule of 3-25 extrafusal m/s fibers.
- Each motor neuron innervate 10- 100 m/s fibres.
- M/s spindles are collection of 6-8 specialized m/s fibres.
- M/s spindles stimulate α -motor neuron.
- Golgi tendon organ activation inhibits α -motor neuron.
- α -motor neuron causes m/s contraction.

Stretch & Inverse stretch reflex

	Stretch Reflex	Inverse stretch reflex
Type of reflex	Monosynaptic	Bisynaptic
1. Stimulus	Tapping of tendon → ↑ in m/s length	↑ in m/s tension
2. Receptor	M/s spindle	Golgi tendon organ
3. Afferent	Ia, II	Ib
4. Centre	Spinal cord	Spinal cord
5. Efferent	A α	A α
6. Response	M/s contraction	M/s relaxation

NERVOUS SYSTEM

Hypothalamus

- Hypothalamic areas & nuclei are :-
 - Preoptic area : Preoptic nu.
 - Anterior (optic area) : Ant., supraoptic, suprachiasmatic

paraventricular nuclei.

3. Middle (tuberal) area : VMN, DMN, arcuate

4. Mamillary area: Posterior, lateral

Hypothalamic nuclei and their functions

Nuclei	Function	Effect of stimulation	Effect of lesion/ destruction
Medial preoptic	Regulates Gn release		
Anterior	Osmoreceptors that sense the osmolality Senses hot and triggers Sweating	Thirst (overhydration)	Dehydration (As in diencephalon damage)
Supraoptic	Water balance through ADH (vasopressin)	--	DI
Supra-chiasmatic	Receive retinal inputs, regulates circadian rhythm / diurnal variation (biological clock)		
Para-ventricular	Oxytocin release, conserve water		
VMN	Satiety centre, glucostat, reward centre, Satiety (fullness); also involved in Aggression	Satiety, aphagia	Hyperphagia (voracious appetite), obesity
DMN	GI stimulation, Triggers Shivering		
Arcuate	Neuroendocrine control, releasing hormone & DA neurons		
Posterior	Thermal regulation by conserving heat	Sympathetic excitation, shivering	Hypothermia (manifested by shivering), sleep
Lateral	Feeding /hunger centre, rage centre	Hyperphagia (voracious appetite), obesity	Anorexia/ starvation, aphagia/ satiety

- Parasympathetic outputs, thirst, diuresis (**Osmoreceptors**), response activated by heat & sleep centre are present in anterior hypothalamus
- Posterior hypothalamus responds to **cold (heat gain centre)** e.g. vasoconstriction, shivering and non-shivering thermogenesis, sympathetic pathway, wakefulness / arousal

- Both the VMN & DMN are involved in appetite control, fat metabolism & control of aggression. Stimulation leads to loss of appetite & **b/L destruction of VMN leads to hyperphagia, hypothalamic obesity** and aggressive behaviour.
 - "Shame Rage" is fear-rage reaction d/to hypothalamic stimulation. Manifestations of fear and rage are seen in decorticate animals.
 - Orexins (hypocretins) are synthesized in neurons located in the lateral hypothalamus. Mutation in one of the orexin receptor genes may lead to **narcolepsy**.
 - Circadian rhythm : is the diurnal variation for many body functions. Seen in secretion of ACTH (which controls steroid secretion), GH, melatonin, gonadotrophins
- Pre-optic nucleus is sexually dimorphic nucleus, contains more neurons in males
 - Thermoregulatory centre is situated in the preoptic area in anterior hypothalamus near the wall of 3rd ventricle.
 - Anti-drop effect of temperature regulation in hypothalamus is mediated by:- serotonin (5-HT)
 - Injection of hypertonic saline in supra-optic nucleus causes--- intense thirst.
 - Injection of hypotonic saline in supra-optic nucleus causes --- Diuresis.

Blood Brain Barrier (BBB)

- Formed by **foot processes of astrocytes** + endothelial cells of brain capillaries having tight junctions
- Lipid soluble substances can cross BBB**
e.g. anesthetic gases (N_2O , Halothane), CO_2 , O_2 unconjugated bilirubin and urea (slowly) – CO_2 most permeable
- Substance which do not cross BBB** - Bile salts, catecholamines, proteins/polypeptide (insulin), 5-HT

- Areas which lie outside the BBB are called **circumventricular organs (CVO)** —area postrema, OVLT, SFO, post pituitary (neurohypophysis) & adjacent ventral median eminence of the hypothalamus
- BBB may be damaged by---anoxia, ischemia, inflammation, hyperosmolality, hypercapnia, acidosis, trauma.

Remember

- Blood nerve barrier is formed by — Perineurium cells
- Blood brain barrier is formed by — Foot processes of astrocytes
- Blood testes barrier is formed by — Sertoli cells

Sensory homunculus (Cortex)

- Located in postcentral gyrus (S_1) & sylvian fissure (S_{II})
- Representation is such that the body appears up side down with foot area on most medial part while face area on lateral part.
- The areas of the body which are very sensitive (rich in receptors) occupy a bigger space like index finger, lower lip etc.
- Trunk & thigh area have small representation

Motor homunculus (Cortex)

- Located in precentral gyrus/ area 4
- Max. representation : Vocalization + Hand
- Body is represented upside down
- Thumb & face** have disproportionately larger area (for precise and delicate control)
- Trunk & lower limbs have disproportionately smaller area

System of fibers	Tract	Sensation carried	Effects of lesion
Anterolateral	Ventral or anterior STT	Crude touch/ pressure	Loss of C/L touch
	Lateral STT	Pin prick/ Pain, temperature	Loss of C/L pain, temp.
Dorsal /posterior columns (Tracts of Goll & Burdach)	1. Fasciculus gracilis (sacral, lumbar region) 2. Fasciculus cuneatus (Thoracic, cervical region)	Fine touch, fine pressure vibration, joint/ position sense	Brown Sequard synd.
Spinocerebellar	SCT	Smoothness and co-ordination of movt (Skilled movements)	

Sleep : stages

Stage	Cl/signs	EEG waves	Eye movt
0 (awake)/ alert state	Eye open	β	Irregular
	Eyes closed	α	
I-NREM	Dozing	$\alpha + \theta$ waves	Bursts of rolling
II-NREM	Equivocal sleep (40-50% of sleep time)	θ , <u>sleep spindles</u> <u>appears</u> k-complex,	α -like bursts
III NREM	Deep / slow wave sleep	θ , δ synchronization	
IV NREM	Deep cerebral/ Slowest wave sleep	δ	Fixed
REM	<i>Paradoxical sleep</i> nightmares	Mixed frequency, Low voltage (θ , $\alpha > \beta$), PGO spikes	Darting movts, active dreaming/

Wave	α	β	δ	θ	γ
Frequency (Hz)	8-13	14-25	0.3-3.5	4-7	>26
Amplitude (Voltage) μV	50-75	20	100	10	10
Stage	0, I NREM	0, I NREM	III, IV NREM	IV NREM	

Location	Parieto-frontal	Frontal		Hippo-campus
Remark	Awake state with eyes closed	Awake / pain with eyes open	Anesthesia	

- NREM starts with α -block
- Delta waves are seen in deep sleep
- In extreme sleep there is absent REM
- Waves recorded during sleep are also known as Buerger's waves
- β wave form is seen during awake / alert state

Disorders of Perception

• Allodynia

Perception of non - painful stimulus (e.g. touch) as painful

• Hyperalgesia

Perception of mild pain as exaggerated.

• Pallesthesia

Ability to feel mechanical vibrations (through Pacinian corpuscles / touch receptors)

• Stereognosis

Ability to perceive shape and size (form and nature) of an object.

- Ability to perceive shape and size is lost (Astereognosis) d/to lesion of tractus cuneatus.
- In Pavlov's classical experiment salivation by dog on seeing food is an innate reflex (unconditioned). And salivation by dog on ringing the bell is only conditioned reflex

Chronic regional pain syndrome (CPRS)

Type	CPRS-I	CPRS-II
Frequency	90% (M/c)	10%
Also k/as	RSD (Reflex sympathetic dystrophy)	Causalgia
A/w	Allodynia	Peripheral nerve injury

Substance P

Pain mediator polypeptide found in intestine, peripheral nerves, many parts of CNS. It is found in high concentration in endings of the primary afferent neurons in spinal cord, nigrostriatal pathway, hypothalamus. It is a probable mediator of Axon reflex (arteriolar vasodilation).

Functions of

Basal ganglia	Planning and programming of voluntary movements, thought is converted into action
Thalamus	Sensory relay station
Hippocampus	Short term memory
Frontal lobe	Self stimulation reward
Cerebellum	Coordination of movements

- Memory is a function of Hippocampus, amygdala and some areas of corpus striatum.

Motor Disorders

Feature	UMND	LMND	Extrapyramidal diseases (EPS)
• Muscle tone	↑ (spasticity)	↓	↑ (Plastic/spastic)
• DTR	↑ (exaggerated)	-nt	N, ↑
• Plantar	Extensor	-	N
• Muscle atrophy	-	+++	-
• Other findings	-	Fasciculations	Involuntary movements (resting and postural tremors)
• Example	Primary lateral sclerosis	Progressive m/s dystrophy	Parkinsonism

- In Amyotrophic lateral sclerosis both UMN and LMN are affected
- Friedrich's ataxia is characterized by extensor plantar and absent DTR despite CST involvement.

BASAL GANGLIA (Basal Nuclei)

- Consist of four nuclei : The caudate nucleus, lentiform nucleus, claustrum and amygdaloid nucleus.
- Amygdaloid nucleus is located in the temporal lobe and has connections with the limbic system. It functionally belongs to limbic system..
- Parts:
 1. *Lentiform nucleus*
Consist of putamen and globus pallidus.
 2. *Corpus straitum*
Consist of caudate nucleus and lentiform nucleus
 3. *Straitum (Neostraitum)*
Consist of caudate nucleus and putamen
 4. *Pallidum*
Globus pallidus is also k/as pallidum becoz it is pale in colour. Glutamate is the predominant NT in globus pallidus interna.
- Main relieving station of the corpus striatum is the striatum but its main output is through the pallidum.
- *Parkinson's d/s* is a/w degeneration of neurons in substantia nigra with resultant depletion of dopamine in corpus striatum. Characteristic triad is cogwheel rigidity + resting tremors + bradykinesia or akinesia.
- *Huntington's chorea* is an AD condition a/w severe degeneration of neurons in striatum (caudate nucleus &

putamen).

- *Sydenham's chorea* or St. Vitus dance is d/to minute hemorrhages and capillary emboli in the corpus striatum. Abnormal movements are similar to Huntington's chorea.
- *Hemiballism* or hemiballismus is d/to lesion in subthalamic nucleus (body of Luys). Proximal movements are affected more.
- *Wilson's d/s* or hepatolenticular degeneration is a AR disease d/to defect in copper metabolism. *Copper content of substantia nigra is high. Lesions are found in lentiform nucleus.*
 - Neurons in the basal ganglia are stimulated mainly by Ach & inhibited by dopamine and GABA.
 - Basal ganglia is involved in the planning & programming of movements.
 - *Pars compacta* of substantia nigra (nigrostriatal pathway) contain dopamine.
 - *Athetosis* is d/to lesion of lenticular nucleus.
 - *Lesion of Red nucleus* : Resting tremor & Lesions of ant. horn : Fasciculation.
 - Lesions of striatum and its connections with thalamus — athetosis and dystonia (cont/L side)

AUTONOMIC NERVOUS SYSTEM

- ANS is responsible for regulation of internal organs & glands, which occur unconsciously.
- ANS comprise sympathetic & parasympathetic nervous systems. ANS includes components of the CNS and PNS that are concerned with the control of visceral functions and thus it is also known as **visceral motor system**. It regulates smooth muscles, cardiac muscles, and glandular activity. It has following components :
 1. The preganglionic fibre arising from CNS (either brain or spinal cord)
 2. The ganglion
 3. The postganglionic fibres supplying to effector organs (smooth muscles or glands)

Parasympathetic NS

- Responsible for stimulation of "rest-and-digest" or "feed and breed" activities that occur when the body is at rest, especially after eating, including sexual arousal, salivation, lacrimation (tears), urination, digestion & defecation. a.

A useful acronym to summarize the functions of the parasympathetic nervous system is SLUDGE (salivation, lacrimation, urination, digestion and defecation, emptying of gastric contents).

- Arise from the CNS with the S2, S3, and S4 spinal nerves and from the 3,7,9,10 cranial nerves. Because of its location, the parasympathetic system is commonly referred to as having "craniosacral outflow". The parasympathetic nerves that arise from the S2, S3, and S4 spinal nerves are commonly referred to as the pelvic splanchnic nerves or the "nervi erigentes".

Sympathetic NS

- In contrast sympathetic NS is responsible for stimulating activities associated with the fight-or-flight response.
- sympathetic NS have "thoracolumbar outflow"

Features	Sympathetic	Parasympathetic
Origin	Thoracolumbar (T1-L2)	Craniosacral (CN III, V, VII, X and S1-S4)
Preganglionic fibres	Short	Long
Ganglia	Present in the vicinity of spinal cord	Present near viscera
Post-ganglionic fibres	Long	Short
Major NT	Noradrenaline	Ach
Major effect	To tackle stress & emergency (fight, fright & fear)	Assimilation of food, energy conservation when person is relaxed
Post-ganglionic fibres	Long	Short
Effect of stimulaⁿ		
- On eyes	dilatation of pupil (mydriasis)	Constriction of pupil (miosis)
- On blood vessels	constriction (↑ in BP)	vasodilatation (↓ in BP)
- On heart	↑ Rate & force of contraction	↓
- On airway/ bronchi	Bronchoconstriction	bronchodilatation
- On g.i. sphincters	Stimulation of sphincters	Relaxation of sphincters

	Sphincters contracts, GI tract relax (↓ peristalsis)	Sphincters relax, contraction of GI tract (↑ peristalsis)
- On GUT	contraction of sphincters Detrusor relaxes ↓ (Urinary retention)	Detrusor contracts, Sphincter relax ↓ (Voids urine)
- Metabolic	Glycogenolysis, lipolysis, gluconeogenesis, ↑ renin, ADH release	
- Salivary glands	↑ secretion	↓ secretion

Neurotransmitters and Neuromodulators

Inhibitory

- GABA is most prevalent inhibitory neurotransmitter in central nervous system (20%)
- Glycine is inhibitory neurotransmitter in brain stem, spinal cord, forebrain, retina & is excitatory for most of the brain.

Excitatory

- Glutamate is major excitatory neurotransmitter in brain/ CNS.
- Aspartate is also excitatory neurotransmitter
- Ach is found in preganglionic ANS endings, postganglionic parasympathetic endings, postganglionic sympathetic sweat glands and vasodilator endings in m/s
- β-endorphins are found in hypothalamus, thalamus, brainstem, retina
- Somatostatin is secreted from median eminence of hypothalamus, substantia gelatinosa, retina

- Glutamic acid is most abundant amino acid in brain
- Pyridoxine is a cofactor for GABA
- Glycine acts on NMDA receptors.
- Dopamine is found to be significantly depleted in the brain of Parkinson's disease (PD) patients and Ach in Alzheimer's disease (AD) patients

REFLEXES AND RECEPTORS

Important Mechanoreceptors

Type of receptor	Location	Sensory modality	Adaptability	Nerve fibres
Non encapsulated receptors				
FNE	Epidermis, cornea, gut, dermis, ligaments, joint capsules, bone, dental pulp	Pain, crude touch, pressure, heat / cold	Rapid	A delta C
Merkel disc	Hairless skin	Touch	Slow	A beta
Hair follicle receptors	Hairy skin	Touch	Rapid	A beta
Encapsulated receptors				
Meissner's corpuscles	Dermal papillae of skin of palm/sole	Touch/tactile	Rapid	A beta
Pacinian corpuscles	Dermis, ligaments, joint capsules, peritoneum, ext.genitalia	vibration	Rapid	A beta
Ruffini ending	Dermis of hairy skin	Stretch (sustained pressure)	Slow	A beta
Neuromuscular spindles	Skeletal m/s	Stretch -m/s length	Fast	A alpha, A beta
Neurotendinous spindles	Tendons	Compression- m/s tension	Fast	A alpha

• Properties of reflexes are --

Stereotyped and specific (Adequate stimulus required), adaptability, habituation, sensitization, final common path

• Monosynaptic reflex	<ul style="list-style-type: none"> • Stretch reflex • Glutamate is neurotransmitter • Receptors are present in intrafusal fibre <div style="text-align: center;"> <pre> graph TD NuBag[Nu. bag fibre Ia / γ] --> IaAfferent[afferent through Ia] NuChain[Nu. chain II, Ia / γ] --> IaAfferent </pre> </div>
• Bi-synaptic reflex	<ul style="list-style-type: none"> • Inverse stretch reflex • Glycine is neurotransmitter (Autogenic inhibition) • Receptors +nt in <u>golgi tendon organ</u> (Ib) • Afferent through Ib
• Polysynaptic reflex	<ul style="list-style-type: none"> • Withdrawal reflex (crossed-extensor) • All superficial reflexes <ul style="list-style-type: none"> – Abdominal reflex – Cremasteric – Babinski sign (flexor withdrawal reflex)

- The first reflex response to appear as spinal shock wears off is often a slight contraction of leg flexors and adductors in response to painful/ noxious stimuli (flexion and adduction or withdrawal reflex)
- Fractionation and occlusion are characteristic of withdrawal response

- Vanilloid receptor (VR₁) are for pain & temperature (> 43°C).
- Two point tactile discrimination is enabled by Meissner's corpuscles. They are extremely sensitive to touch and are rapidly adapting mechanoreceptors
- Hair cells (present in organ of Corti) are receptors of hearing (auditory receptors).
- Rods and cones are photoreceptors present in retina.
- Glomus cells are chemoreceptors present in carotid and aortic bodies
- Pacinian corpuscles and Ruffini endings lie deep to skin in the dermis, their receptive fields are large. Pacinian corpuscles are useful mainly for appreciation of vibration. Ruffini endings respond to stretching of the dermis
- In contrast to above Merkel's cell receptors and Meissner's corpuscles have small receptor fields (esp. over fingers) and allow good tactile localization.

• Properties of receptors are ---

- Specificity, adaptation, sensory coding, specificity of response (law of adequate stimulus), law of projection, law of intensity discrimination (recruitment of sensory units)
- All sensory system code for 4 elementary attributes of a stimulus --- modality, location, intensity, and duration.
- Cough receptors : within sensory distribution of 5th, 9th, 10th cranial nerves . Present on external auditory meatus, wall of pharynx, trachea, bronchi (but not on palate & uvula).
- Taste receptors : Present on tongue, epiglottis, esophagus, larynx and hard palate.

Baro & Chemo Receptors

Name	Location	Stimulus	Afferent	Integration/Efferent	Response
Baroreceptors					
Arterial	Carotid sinus-9th nerve Aortic arch-10th nerve	\uparrow BP*	CN 9,10 NTS	Buffer n. (br. of vagus)	\downarrow sympathetic vasoconstrictor tone
CVP receptor	Lt. atrium, Pulmonary veins, wall of SVC/Jugular veins		CN10		\downarrow sympathetic discharge to heart
Chemoreceptors					
Central	Medulla	CO_2 can cross BBB & generate H^+		Medulla	Hyperventilation
Peripheral	Carotid body (located at bifurcation of CCA) Aortic bodies	\uparrow H^+ (acidosis) \downarrow PO_2 (hypoxia) \uparrow CO_2 \uparrow H^+ (acidosis) is the most potent direct stimulus		VMC	Hyperventilation Vasoconstriction (\uparrow CO, \uparrow HR, \uparrow BP)

- Baroreceptor signal at BP range 50-150 mmHg.
- When carotid sinus nerve is severed (sectioned) → loss of inhibition on VMC → \uparrow sympathetic discharge → vasoconstriction \uparrow BP, \uparrow HR, \uparrow COP.
- If carotid artery is ligated above the level of carotid sinus There will be → \downarrow BP, \downarrow HR, & fainting (carotid sinus syndrome).

- Supportive reaction (+ve & -ve), magnet reaction & stretch reflex are integrated in spinal cord.

- Human body is maintained in an upright balanced position because of integrity of the postural reflex arc.

Imp .Reflexes

Reflex	Loca ⁿ of receptors	Stimulus	Response
Cushing Reflex	VMC	\uparrow ICT (> 33 mmHg), \downarrow CBF \downarrow blood supply to VMC	\uparrow systemic BP, Bradycardia, bradypnea
Bainbridge	RA/ vena cavae	Rapid infusion of blood/saline \downarrow Atrial distension	Reflex tachycardia
Bezold-Jarisch Coronary Chemoreflex	LV	Inj. of 5-HT, Veratrum capsaicin, nicotine in coronary artery	Apnea, \downarrow BP, \downarrow HR, Tachypnea later on
J. Reflex/ Pulmonary chemoreflex	Juxtacapillary in walls of alveoli, C-fibres	Hyperinflation of lung (normal inspiration)	\downarrow BP, \downarrow HR,
Hering Breuer inflation	Airway	Steady lung inflation	\uparrow expiration
Hering Breuer deflation	SM Cells	Mark deflation of lung	\downarrow expiration

Integration of Cortical/ Brain Stem Reflexes

- Optical righting reflexes, hopping & placing reaction are integrated in cerebral cortex.
- Other righting reflexes are integrated in midbrain.
- Tonic neck reflex & tonic labarynthine reflexes are integrated in medulla.

Neural Reflexes

Reflex	Afferent	Integrated in	Efferent
• Swallowing (Deglutition)	5, 9 10	Medulla (NTS, Nu Amb)	5, 7, 12
• Gag	9	Nu. ambiguus	10
• Corneal/ conjunctival	CN-5 ophthalmic div ⁿ	Pons	7
• Stapedial	8, Auditory div ⁿ	Pons	7 (facial)

- Absent corneal reflex is most sensitive indicator of trigeminal nerve damage.
- Masseteric reflex (jaw jerk) is a monosynaptic stretch reflex for masseter m/s. On percussion of the jaw proprioceptive impulses are carried via 5th CN and relayed to mesencephalic nucleus of trigeminal nerve, which sends excitatory impulses to the motor nucleus of CN 5 and efferents from here produces jerk.

Pupillary pathway of Light Reflex

Afferent

light → Optic nerve → Optic chiasma → Optic tract
Contraction (constriction in response to light)

↓
Superior Colliculi
↓
Pretectal region
↓
EWN
↓

Sphinctor ← Short ← Ciliary ← Oculomotor N
(pupillary) Ciliary N ganglion

← Efferent

CVS

Jugular Venous Pulse (JVP)

- The normal JVP consist of 3 positive waves (a, c, and v) and 2 negative waves (x and y)
- Cannon waves** (Very large/giant 'a' waves are d/to atria contracting against closed tricuspid valve)
 - (a) Regular in Junctional rhythm
 - (b) Irregular in complete heart block, multiple ectopics, A-V dissociation with VT.
- In AF : a-wave & x-descent are absent & v wave and y ↑
- In severe TR : Prominent v-wave + obliterated x-descent

- **Kussmaul's sign** is an inspiratory ↑ in JVP. Seen in constrictive pericarditis & restrictive cardiomyopathy, RVF, RV-infarct
- **Friedreich's sign** is the rapid fall (steep 'y' descent) and rise of JVP seen in constrictive pericarditis & TR
- **Abdominal jugular reflux** is +ve in Rt heart failure & TR. Suggest ↑PCWP or ↑CVP -ve in Budd Chiari syndrome
- M/c cause of raised JVP is CCF
- Normal upper limit of JVP above the sternal angle is 4 cms
- 'a' ascent is d/to continuous diastolic inflow of blood into great veins, RA & RV.

	'a' wave	'c' wave	'v' wave	'x' wave	'y' wave
Also k/as	atrial wave	closure wave	Passive process	x- descent	y descent
D/to (Physiology)	Rt atrial contrac ⁿ	D/to bulging of TV carotid a. impact on JV, retrograde transmi ⁿ	Rt atrial filling	Chordal pulling of tricuspid ring (displacement of TV), atrial relaxation	Opening of TV(tricuspid valve)
Relation	precedes S1	succeds S1		precedes S1	succeds S2
Absent in	AF		SVC obstruction	TR, AF	
Diminished in	Tachycardia Prolonged PRi				slow in TS, RVH, RA myxoma
Large in	Atria contracting against pressure (TS, Tr. atresia Rt atrial myxoma PS or PAH, Ebstein anomaly)	TR	AF, TR	↑in /Steep in constrictive pericarditis, tamponade, restrictive CMP	Sharp/ steep in TR, AF, const pericarditis, restrictive CMP
Other	Canon waves (Atria contracting against closed TV) in AV dissociation, complete ht block			Reversed x-descent in TR	

Heart sounds

	1st	2nd	3rd	4th
D/to	Closure of MV & TV	Closure of aortic & pulmonary valves	Tensing of papillary m/s or chordae tendineae	when atrial pressure is high (represent atrial contra ⁿ)
Duration	0.15 Sec.	0.12 Sec.	0.1 Sec.	
Frequency	25-45 Hz (ave. 30 Hz)	50 Hz.		
Coincides with ECG	R-wave	End of T-wave	Beginning of P-wave	P-wave
Coincides in JVP	C-wave	Begining of v-wave	End of v-wave	a-wave
Other events	Isovolumetric contraction occurs during start of ventricular systole	Dicrotic notch in aortic pressure curve	Vent./first (early) rapid filling phase	when ↑ resistance to ventricular filling
Loud in /Heard in	Sinus tachy, MS, TS, High output states, short PRi		Heard in Severe MR, CCF, TR <30 yr., Cons. pericarditis	Heard in HTN, AS, HOCM, AS, acute MI, MR
Soft in /Absent in	Prolonged PRi, severe MS, emphysema, obesity		Severe MS (Absent S3)	Atrial fibrillation (Absent S4)
Split in	RBBB, AV block, AF, Ebstein's, myxoma	RBBB, ASD, TAPVC (wide & fixed), LBBB, Severe AS, HOCM, CoA, HTN (Reverse/paradoxical split)		

Name of phase	Duration (Sec)	Atrial pressure change	Ventricular pressure change	Aortic pressure change	ECG	Change in heart valve	Volume change of ventricle
1. Isovolumetric contraction	0.05	↑P, ↑V (bec AV valve bulges in atria) "c-wave" in JVP	↑P upto 80 mmHg (In LV) Length (size) of ventricle is const. Press in RV ↑se upto 10 mmHg	No change (remains 80 mmHg)	Later half of R-wave S1	Semilunar v closed AV are closed (not firmly) at the end ao & pv open	Vol. 100 → 130 ml
2. Rapid ejection phase	0.10	No change (P=0 mmHg) Atrial vol ↑es	Pressure ↑se (In LV) & reaches upto or possibly > 120 mmHg maximum Press. in RV reaches 25 mmHg (peak)	↑se aortic press [↑se 1st & then to pump the blood into aorta vent. p have to ↑se simultaneously]	ST segment	Onset is marked by opening of SLv (aortic & pulmonary) AVv are firmly closed	Vol ↓es & reaches upto 65 ml
3. Reduced ejection phase	0.15	(P = 0 mm Hg)	Pressure starts ↓ing & drops upto 80 mmHg	↓es & reaches to 80mm Hg	T-wave (Later half)	SLv open AVv are closed	Vol ↓es upto 50 ml
4. Protodiastole	0.04 (shortest phase)	Slightly ↑es pressure	↓ P further (already falling ventricular pressure drops more rapidly)	Slightly ↑ & diastolic notch appear d/to sharp closure of sl valve at the end	----	SLv open AVv closed at the end sharp closure of aov produces incisura	Vol. still 50 ml
5. Isovolumetric relaxation	0.06	Press. ↑es "v-wave" comes in JVP	P ↓es It ends when ventricular pressure falls below atrial pressure & AVv open	P = 80mmHg	isoelectric line in ecg S2	AV-valve open at the end of phase (opening snap) SLv closed	V = 65 ml
6. Early Rapid filling phase (Passive filling of ventricle)	0.10	Press. ↑es	P = 0mm Hg	P = 80mm Hg " S3	AVv open SLv closed	V = 85-90ml
7. Diastasis/reduced filling phase of ventricle (Active filling)	0.20 (longest phase)	No change (P = 0 mm Hg)	P = 0 mm Hg or low	Press ↓es from 80 to 65mm Hg " S4	AVv open SLv close	Vol reaches upto 100ml
8. Last/rapid filling phase of ventricle (Active filling) Atrial systole	0.10sec	↑P "a - wave" comes in JVP contraction of atria	P = 0mm Hg	Pressure same	P-wave S4	AVv open SLv close	Vol. 100-130ml

CARDIAC CYCLE

- Total duration of cycle is 0.8 sec.
There are 2 main phases -
Ventricular systole + Ventricular diastole
(1, 2, 3) \Rightarrow 0.3 sec (4, 5, 6, 7, 8) \Rightarrow 0.5 sec
- Atrial systole is very short (0.10 sec), seen in phase 8.
- **Electro-mechanical systole** (QS_2 interval) is the period from beginning of the QRS to the aortic component of S_2 .
- Phase of minimum motion of heart : Mid-diastole.
- When HR is low-- duration of diastole \uparrow & AV-valves drift towards the closed position.
- During exercise the diastole is shortened $>$ systole.
- 70% of ventricular filling occurs passively during Ventricular phase of diastole (In phase 6 & 7).
- In mid diastole or isovolumetric relaxation phase, there occurs \max^m drop in pressure. Stroke volume & work done are least.
- Coronary blood flow (to the left ventricle) \downarrow es dramatically during the isovolumetric phase of systole, prior to opening of the aortic valve. CBF is \max^m during early diastole phase of cardiac cycle.
- Coronary circulation is regulated by **autoregulation**.
- **Incisura** — In protodiastole sharp closure of aortic valve produces incisura in aortic pressure curve
- **Dicrotic notch** is d/to closure of aortic valve in early rapid filling phase. Incisura is small or absent in small/calcified aortic valve (AS)

Blood Pressure (BP)

- BP is *spuriously high* in
Rigid / calcified vessels (e.g. Monckberg's sclerosis), diabetics, elderly, use of small cuff, and in obesity
- SI unit of BP measurement is ---KPa
- **Methods of BP recording**
 1. **NIBP** (Non-invasive) : Using sphygmomanometer.
 2. **IBP or ABP** (Invasive) : Most accurate method of BP recording. Artery is directly catheterized & connected to a manometer/monitor.
- **Korotkoff's Sound** are produced by turbulent flow in the brachial artery. Sounds again reappear at lower pressure (**Auscultatory gap**). Palpatory method is used to avoid this.
- Normal value of BP is 120/80 mmHg or 16/10.64 kPa
- Pulse pressure is the difference b/w SBP & DBP.
 $PP = SBP - DBP = 40 \text{ mmHg}$
Determinants of PP
 1. Stroke volume ($\uparrow SV \rightarrow \uparrow PP$) as in AR
 2. Arterial compliance $\Delta V / \Delta P$: (\downarrow compliance $\rightarrow \uparrow PP$).

Aorta and large arteries are more compliant, so PP is less.
 \max^m PP is seen in dorsalis pedis artery.

Mean Arterial Pressure (MAP)

is the average pressure throughout the cardiac cycle.

$$MAP = DBP + 1/3 PP = 1/3 (2DBP + SBP) \Rightarrow 95 \text{ mm Hg}$$

- D/to gravity pressure, BP in any vessel below heart level is \uparrow ed & in any vessel above the heart level is \downarrow . This gravitational effect is 0.77 mmHg/cm of vertical distance. In the upright position, when the MAP at heart level is 100 mmHg, the MAP in a large artery in head (50 cm above heart) is 62 mmHg.
- **Mean circulatory filling pressure** is the arterial pressure taken at the point where heart stops beating.

Cardiac Output (COP)

- Output of the heart per minute. In resting supine man it is 5 L/min.

• **Factors affecting CO** $CO = SV \times HR$

\uparrow	No change	\downarrow
– Late pregnancy	– Sleep	– Sitting/standing
– Eating	– Moderate change in temperature	from Lying position
– Histamine, Adr	environment	– Rapid arrhythmias
– Anxiety/excitement		

$$\text{Pressure} = \text{Flow} \times \text{Resistance}$$

$$\text{Systemic BP} = \text{Systemic Blood Flow} \times \text{PR}$$

$$\text{Cardiac work} = \text{Stroke work} \times \text{HR} = SV \times MAP \times \text{HR}$$

• **Cardiac Index**
$$\frac{CO}{\text{Body surface area}} = \frac{SV \times HR}{BSA}$$

$$\Rightarrow 3.2 \text{ L/min / sq.m of body surface}$$

Ejection fraction (EF)

Percentage of end-diastolic ventricular volume that is ejected with each stroke. Normally it is $> 65\%$

$$EF = \frac{SV}{EDVV} = \frac{70 \text{ ml}}{130 \text{ ml}} = \frac{\text{Amt. of blood ejected}}{\text{Amt. of blood received}}$$

EDVV is about 130 ml. Thus 50 ml blood remains in each ventricle at end of systole (end systolic vent. volume)

- **Stroke volume (SV)** is amount of blood pumped out of each ventricle per beat. 70 ml (in resting supine man). SV

is an important determinant of cardiac output and is also used to calculate ejection fraction

$$SV = CO / HR$$

$$SV = EF \times EDV$$

- SV depends on several factors such as heart size, contractility, duration of contraction, preload (EDV), and afterload.
- Sterling's law**: SV within its limits correlates **directly** with the end diastolic fiber length or volume (preload or EDV) & **inversely** with the arterial resistance (afterload).

Venous Return (VR)

- Input of heart per minute.
- Factors increasing VR**
 - Sympathetic stimulation (venoconstriction).
 - ↑ Blood volume.
 - Standing from lying.
 - Respiration pump (deep inspiration)
 - Skeletal m/s pump (Calf pump), deep fascia.
- Arterial pressure has nothing to do with VR.

Cardiac Fibres

There are two type of cardiac fibres

- Automatic**: These are excitable (working) tissues in which AP (depolarisation) is d/to Ca^{++} ions. Depolarization is slow in the beginning but because of explosive Na^+ entry firing occurs & sharp upstroke develops. **Repolarization is rapid**. Plateau phase is absent e.g. SAN, AVN (i.e. pacemaker cells), Purkinje fibres.
- Non-automatic**: In these fibres AP is d/to Na^+ ions. Depolarization is very rapid and repolarization is slow. Plateau phase is seen.

- Transmembrane potential in ventricular muscles**:

Event/Phase	Stage	d/to
Depolarization phase	0 (Rapid d~)	Na^+ influx
Repolarization	1 (early / rapid)	Closure of Na^+ channel, Cl^- influx
	2 (Plateau / sustained)	Ca^{++} influx (slow) K^+ efflux
	3 (Late r~)	K^+ efflux (closure of Ca^{++} channels)
	4 (full r~)	K^+ efflux continued, resting potential restored

- Depolarisation is slow in diastole (from -90 to -60 mv) after stage 4, called **prepotential/ pacemaker potential**. Prominent prepotential is d/to ↓ in K^+ efflux, opening of h/f channels, & Opening of T-type Ca^{++} channels.

- Order of Ventricular depolarization**:

- Endocardial surface of IVS (Lt) → (Rt)
- Epicardium →
- Topmost portion of IVS (septum), base of the heart & the pulmonary conus are **last to be depolarized**.

- Order of Ventricular repolarization**:

- The apical endocardial surface (first)
- The base of the endocardial surface (last)

- Conduction velocity (speed)** is fastest in purkinje system (4m/s) and slowest in AV nodes

N/s OF HEART

Parasympathetic / Effect of vagal stimulation

Rt Vagus supplies SA node. **Lt vagus** supplies AV-nodes, Its stimulation causes when stimulated it slows AV conduction



Sinus bradycardia



AV - block precipitated

- Acetylcholine acts on heart via activation of K^+ channels.

Sympathetic effect on heart

Most sympathetic fibres come from stellate ganglion
stimulation of right stellate ganglion



↑ HR by increasing SAN discharge

Stimulation of left stellate ganglion



Shortens AV conduction time & refractoriness
(↓ AV nodal delay)

Sympathetic effect on heart

- ↑HR → +ve chronotropic effect
- ↑es force of cardiac contraction --- +ve inotropic effect
- ↑es the rate of transmission in conducting fibres --- +ve dromotropic effect.

Effects of denervation of heart :

- In humans in whom both NA and cholinergic fibres are blocked HR ↑es to 100 bpm, SAN starts generating its normal intrinsic rythm which is 100 bpm.
- Pulmonary artery pressure increases far less than COP d/to opening of new collaterals.

CVS changes during inspiration -

- Venous pressure falls - 2.5 to - 6 mm Hg d/to \uparrow in negative intrathoracic pressure.
- Physiological splitting of S_2 (reduplicated S_2)
- **Pulsus paradoxus** (fall in SBP ≥ 8 mm Hg)
- \uparrow HR (sinus tachycardia) because impulses from vagal stretch reflex stimulate receptors in lung \rightarrow inhibit cardioinhibitory area in medulla.
- \uparrow VR, CVP drops from 6 mm \rightarrow 2 mm Hg

CVS/ respiratory changes during exercise

- \uparrow HR (sinus tachycardia)
- Diastole is shortened much more than systole
- There is \uparrow extraction of O_2 from the blood and increased ventilation in exercising muscles. There is \uparrow A-V O_2 difference (resting 5 ml/100 ml \rightarrow 16 ml/100ml).
- **Cardiac output, venous return, stroke volume, PP, SBP and pulmonary artery pressure all are \uparrow ed**
- Values which \downarrow se : Peripheral resistance, afterload, and DBP in severe exercise.
- Strenuous exercise can cause *lactic acidosis* and *hyperkalemia* by releasing K^+ from skeletal m/s.
- Hypercapnea, oxygen debt.
- **In moderate exercise** the abrupt \uparrow se in ventilation is d/to psychic stimuli & afferent *proprioceptive* impulses from muscles, tendon and joints. Arterial pH, pO_2 , pCO_2 remain constant as ventilatory drive \uparrow es O_2 consumption
- Blood flow to
 1. Brain (750ml), skin (500 ml/min) remains unchanged
 2. Kidney, liver, GIT \downarrow es
 3. Heart (250 \rightarrow 1000 ml/min.), lungs and *active* skeletal m/s (650 \rightarrow 20,000 ml/min.) \uparrow ed.
- *Isometric versus isotonic exercise*

Feature	Isometric	Isotonic
• Main aim	\uparrow Muscle bulk	\uparrow Muscle power/ endurance
• Cardiac work load	More	Less
• HR	\uparrow	Prompt \uparrow
• COP	\uparrow	\uparrow
• SBP	Sharp \uparrow	\uparrow moderately
• DBP	Sharp \uparrow	Unchanged or \downarrow
• Stroke volume	Little change	Marked \uparrow
• TPR	\uparrow (d/to compression of vessels & \downarrow blood flow in m/s)	\downarrow (d/to vasodilation in exercising m/s & \uparrow blood flow in m/s)

Type of M/s Fibres & major Fuel Sources in

Features	Type-I	Type-II
• Fibres type	Oxidative, slow more mitochondria	Glycolytic, fast, more enzymes)
• Excitability	Easy to excite	Difficult to excite
• Fatiguability	Less	More
• M/s glycogen depletion	Slow	Fast
• Used in	Marathon runner	Sprinter (100 m runner)
• Major fuel source	ATP (Derived from blood glucose + FFA) is major source throughout	Cr-Phosphate (first 4-5 s)
• Glucose is derived from.	Blood glucose - 4 min Liver glycogen - 18 min M/s glycogen - 70 min TG of fatty tissue - 4000 min.	M/s glycogen and metabolized by anaerobic glycolysis

- **BNP** (Brain natriuretic peptide) is a marker of myocardial dysfunction. Degraded and eliminated from plasma by neutral endopeptidases.

CVS Changes in athletes/ physically trained

- Maintains high CO at lower HR because of high vagal tone (**sinus bradycardia**).
- Greater ESVV (end systolic ventricular volume)
- Greater stroke volume at rest

Changes during supine (lying) to prone position

- Significant volume of blood pools in the lower limbs d/t high compliance of LL veins, thus VR decreases
- \downarrow in VR & EDVL --- Stroke volume & COP \downarrow es

Effects of CSM (Carotid sinus massage)

Cardio-inhibitory response: \downarrow in both sinus rate, atrial rate and AV-nodal conduction.

Effects of Valsalva Maneuver (Valsalva)

Venous compression, and the accompanying large increase in right atrial pressure, impedes venous return into the thorax. Reduced filling and preload leads to a fall in cardiac output.

- Afterload depends upon --- arterial resistance (\uparrow es in systemic HTN)
- Preload depends upon --- EDVV (or end diastolic fibre length)
- SBP depends upon --- contractility (pumping power) of heart
- DBP depends mainly upon TPR
- In systole coronary blood flow falls by 40%
- Lt atrial filling pressure closely approximates PCWP (3-8 mmHg normally)
- SA node is called pacemaker because it initiates the impulse at faster rate

BLOOD VESSELS & BLOOD FLOW

Viscosity

- Viscosity mainly depends upon hematocrit & also on plasma proteins fibrinogen & globulins.
 - Viscosity \uparrow in :
 - Disorders in which plasma proteins such as the immunoglobulins are markedly elevated (e.g. multiple myeloma, Waldenstrom macroglobulinemia)
 - Hereditary spherocytosis (abnormal rigidity of RBCs)
 - In polycythemia (\uparrow hematocrit)
- [Conversely, in anemia peripheral resistance and viscosity decreases.]

Resistance

- The resistance to blood flow. At any given pressure drop, the flow rate is determined by the resistance to the blood flow. The vessel diameter (or radius) is the most principal determinant of resistance in blood vessels.

1. Radius (inversely related to fourth power of the radius)

2. Viscosity (directly related)
$$R = \frac{8nL}{\pi r^4}$$

- Normal blood flow is streamline (laminar). Turbulent blood flow is more common in anemia

Resistance R \propto Viscosity

$$\propto \frac{1}{r^4}$$

Viscosity \propto Hct

Average velocity \propto

$$\frac{F(\text{Flow})}{A} = \frac{\Delta P}{RA}$$

[A = total cross sectional area, P = Pressure]

- Small airways has laminar flow because diameter is very small, velocity is low and Reynold's number is <2000 .

- Resistance to blood flow is directly proportional to viscosity & inversely related to radius⁴
- Viscosity depends mostly on hematocrit
- Velocity of blood depends upon total cross sectional area (inversely related)
- In arterial blood Hct are 3% less than venous blood
- In capillary blood Hct are 25% less than venous blood (d/ to plasma skimming)
- Max^m blood is contained in venules (54%)
- In systole coronary blood flow falls by 40%.
- Blood loss upto 20% of bld volume is tolerated normally by redistribution of bld flow mediated by vasospasm
- In a healthy patient blood volume must fall by 30-40% before hypotension occur

• Order of Velocity of Blood

= Aorta > Vena cava > artery > arteriole > capillaries

• Order of Cross sectional area

= Capillaries (maximum) > arteriole > artery > Vena cava

- Vasoconstrictⁿ \uparrow the velocity of blood flow & produces turbulence e.g. bruits heard over arteries d/to atherosclerotic plaques & Korotkoff's sounds

Triple Response of Lewis

- Develops when skin is stroked firmly
- Mediated primarily by histamine (originally called H-substance) and related peptides
- Immediately there is

$$\text{red reaction} \xrightarrow{\text{in } 1/2 \text{ min}} \text{Flare} \longrightarrow \text{Wheal}$$
- Red reaction (red line) is d/to --- histamine mediated relaxation of precapillary sphincters
- Flare reaction (Flush, Axon reflex) is d/to --- substance P mediated arteriolar dilatation
- Wheal (skin edema) is d/to --- histamine mediated increased capillary permeability.

→ Triple response is present after total sympathectomy.

→ Flare is absent in locally anesthetized skin.

Cerebral Blood Flow (CBF)

- CBF is virtually constant despite changes in arterial BP. In moderate exercise there is no change in CBF. autoregulation maintains CBF at BP of 65-140 mmHg.
- CBF is insensitive to hormones and sympathetic nerve activity.

Condition	CBF mL/100g/min	O ₂ delivery rate mL/100g/min
• Normal	50	10
• Ischemia starts	20	4
• Critical level	10	2

- Factors controlling CBF :
 1. PCO_2 : Most important
 2. Acidosis (H^+) : direct stimulus
 3. PO_2
- High O_2 tension in inspired air (PO_2), produces cerebral vasoconstriction and thus \downarrow CBF. However this is protective as this reduces O_2 toxicity

- $CBF \propto PCO_2$. If PCO_2 is raised upto 80 mm Hg, CBF will be doubled (d/to cerebral vasodilatation)
- Vasodilatation produced by CO_2 is max^m in brain & skin.

- Blood flow in ml/min to various organs

L	K	M	B	S	C
1500	1250	850	750	500	250

[Mnemonic: Lali ki maa BSC :

Liver /kidney/muscle/brain/spleen/cardiac]

- Maximum O_2 consumption
Cardiac m/s 9.7 ml/100 gm/min & Liver 51 ml/min

Factors affecting Caliber of Arterioles

Constrictors

1. Adrenaline (in rest)
Nor adrenaline (always)
2. Serotonin
3. ADH/ AVP, Angiotensin-II
4. Neuropeptide Y
5. Endothelin-1 (most potent)
6. \downarrow local temperature
7. $\uparrow Ca^{++}$

Dilators

1. Adrenaline in liver
2. Substance P
3. Histamine
4. ANP, VIP, CGGRP α , NO
5. Kinins (Bradykinin)
6. $\uparrow CO_2$, $\downarrow O_2$, \uparrow temp, \downarrow pH,
 \uparrow lactate (Acidosis)
7. $\uparrow K^+$, $\downarrow Ca^{++}$, \uparrow adenosine

- Adenosine have vasodilator role in cardiac ms but not in skeletal ms.
- Endothelin-1 is the most potent vasoconstrictor Endothelin-1 > Angiotensin-II > Renin
- Most of the factors which causes vasodilatation in systemic circulation causes vasoconstriction in lungs (eg. Vagus stimulation & Hypoxia, Histamine causes pulmonary vasoconstriction).

RESPIRATORY SYSTEM

• Characteristic of Pulmonary Circulation

- Mean pressure difference of arteries is low.
- Arterioles are not present in lung, So resistance is low, capillary pressure is low.
- Can accommodate large amount of blood volume. Receives volume equal to cardiac output.
- Hypoxia & acidosis produce vasoconstriction & \uparrow pressure in pulmonary vasculature ($\downarrow PO_2 \rightarrow \downarrow$ es K^+ efflux through O_2 sensitive K^+ channels \rightarrow depolarisation). All other factors produce vasodilation in pulmonary circulation. [Hypoxia & acidosis \downarrow systemic BP by vasodilatation . Mechanism is K^+ efflux through ATP sensitive channels \rightarrow hyperpolarisation].
- Pulmonary arteries are more distensible than systemic.

Lungs: General consideration

- In normal adults lung is kept dry bec/ of hydrostatic pressure.
- Both lungs and thoracic cage are elastic structure
- During quiet respiration intrapleural pressure is -3 to -5 mm of Hg. **On inspiration it becomes more negative** (upto -30 mm Hg on a strong inspiratory effort)
- Intrapleural pressure is negative d/to lymphatic drainage of pleural cavity. It is the major factor preventing the lungs from collapsing. If the intrapleural pressure became equal to atmospheric pressure the lungs would recoil and collapse.
- Presence of cartilage in the upper airway is responsible for maintaining the airway.
- **Clara cells** are non-ciliated cells present in terminal bronchioles. Their role in decreasing surface tension, stem cell function, protection against emphysema and harmful substances has been described.

Lung volumes and spirometry

	Volumes	Values in male	in female	
Inspiratory capacity (IC)	IRV	3.3	1.9	Vital capacity (VC)
	TV	0.5	0.5	4.8 L in male
Functional residual capacity (FRC)	ERV	1	0.7	
2.2 L in male	RV	1.2	1.1	
1.8 L in female				

TV

Volume taken in or out in quite respiration. Normally it is 5-8 ml/kg in children or 500ml in adults.

RV

Volume remaining after forceful expiration which can not be exhaled (trapped air in alveoli). V

Volumes such as RV & TLC cannot be measured with the spirometer but require an additional measurement technique, either the body plethysmograph or helium dilution in order to be determined

FRC (ERV + RV) :

Volume of air remaining after normal expiration.

RV (and thus FRC also) is measured by body plethysmograph, helium dilution method & N_2 washout method.

FRC is ↑ed in conditions a/w hyperinflation e.g. emphysema, asthma, atelectasis, and old age.

ERV

Volume expired forcefully after & above normal expiraⁿ.

Parameter	Also k/as	Formulae	Normal value
Minute ventilation (MV)	Total pulmonary ventilation	$MV = TV \times RR$	6 L/min
Alveolar ventilation		$(TV - DS) \times RR$	4.2 L/min

Measurement of expiratory flow is extremely useful to us particularly in identifying obstructive lung disease.

→ Rapid, shallow breathing causes : ↑ RR, ↓ TV

→ Slow, deep breathing causes : ↓ RR, ↑ TV

Maximum breathing capacity/ Max^m voluntary ventilation volume MVV = 125 to 170 × RR

Pulmonary reserve or breathing reserve (PR)

Maximum amt. of air above the pulmonary ventilation, which can be breathed in and out

BR = MVV - PV

Dyspnoeic index is % pulmonary reserve. > 60% is normal

Work done in Normal breathing : 0.5 kg - m/min &

Maximum work of normal breathing : 10 kg - m/min.

Airflow/airway Resistance

Most of the resistance to airflow occurs in the first few divisions of the airways. The more distal airway divisions, because of their large cross-sectional area, constitute a silent zone of airway resistance.

Resistance to airflow ↑es in lung secretions, edema, lower

lung volumes, obstructive d/s like emphysema.

Resistance in large (upper) airway is measured by --- inspiratory flow curve or flow volume loop.

Airway resistance is predominately contributed by first few divisions (medium size bronchi).

MMEFR (Maximum Mid-expiratory flow rate) or FEF_{25-75%} is optimal/ sensitive test for resistance in small airways

More resistance in expiration / at the end of expiration is d/ to --- Dynamic collapse of airways.

→ Any capacity which includes RV can't be measured by spirometry. So RV, FRC, and TLC can not be measured by spirometry

→ FEV₁ is normally 80% of FVC. FEV₁ is most reproducible index of severity of obstruction

→ Response to bronchodilator therapy is assessed by --- PEFr

→ PEFr is probably the single best test for measurement of ventilatory efficiency.

→ TVC (Timed vital capacity) is used to distinguish b/w obstructive & restrictive d/s

→ In plethysmography, on expiration against closed glottis pressure increases both in lungs as well as in box.

Closing Volume denotes resistance in small airways. CV is the lung volume at which respiratory bronchioles/alveoli start collapsing particularly during forced expiration.

CV = Closing capacity - RV

Closing Capacity CC = CV + RV

Closing capacity is high in emphysema

Lung compliance

Is the change in lung volume per unit change in airway pressure. Measured as L/ cm of H₂O

↑ ed in --- Obstructive diseases like emphysema

↓ ed in --- Restrictive diseases e.g. pulmonary fibrosis, pulmonary edema, ILDs

$$\text{Compliance } (C_L) = \frac{\Delta V}{\Delta P} \quad \text{Resistance } R = \frac{k.L.\eta}{\pi r^4}$$

→ HMD is a/w ↓↓ in compliance without any change in resistance

→ MAS is a/w ↑↑ in resistance with some ↓ in compliance

→ Stability to alveoli is provide by --- compliance of lung tissues, surfactant

→ FRC is low in --- Pulmonary edema, RDS/HMD, pneumonitis

Pattern of Respiratory D/S (Interpretation of PFT's)

Obstructive		Restrictive	
Hallmark is \downarrow FEV ₁		Hallmark is \downarrow TLC	
\downarrow FVC or VC, \downarrow PEF, \downarrow MVV		Normal or \downarrow PEF, \uparrow MVV	
\downarrow FEV ₁ /FVC (<70%)		Normal/ \uparrow FEV ₁ /FVC (>80%)	
N, \uparrow Compliance, \uparrow RV, \uparrow RC		\downarrow Compliance, normal RV	
Acute	Chronic (COPDs)	Parenchymal	Extra-parenchymal
Asthma	Chr. bronchitis	(ILDs)	<u>Neuromuscular</u>
Bronchiolitis	Emphysema	Sarcoidosis	Diaphragmatic paralysis, MG, Cervical spine injury
Bronchiectasis		Idiopathic pulm. fibrosis	M/s dystrophies
Cystic fibrosis		Pneumoconiosis	
		Drugs, Radiation induced ILDs	<u>Chest wall diseases</u>
			Kyphoscoliosis, obesity, ankylosing spondylitis, polio

Respiratory Reflexes

- **Hering Breur inflation reflex**
Whenever there is hyperinflation of lungs (>1.5 L), it causes \rightarrow \uparrow in expiration time.
- **Hering Breur deflation reflex**
Whenever there is marked deflation of lungs, it causes \rightarrow \downarrow in expiration time. This reflex is important in preventing atelectasis.
- **Head's Paradoxical reflex**
Inflation of lungs induces further inflation (d/o elastic recoil of alveoli). Plays important role in initiation of respiration in newborn babies.
- **J-receptor (Juxta capillary) reflex**
Also k/as **pulmonary chemoreflex**. Activated in pulmonary congestion, embolism, & edema. Stimulatⁿ of J-receptors (as in injection of serotonin & capsaicin in lungs) causes apnea f/b rapid & shallow breathing, brady, \downarrow BP.

Pneumocytes/ Alveolar cells

Type I : Primary lining cells of alveoli, most numerous. Probable role in phagocytosis.

Type II : Granular pneumocyte, contain multilamellar bodies, secrete surfactant

Type III : doubtful role, also k/as **Brush cells**

- \rightarrow **Dust cells** are macrophages in the wall of alveoli. They phagocytize dust particles in their cytoplasm
- \rightarrow In CHF these macrophages phagocytose erythrocytes that escape from capillaries. The cell acquire brick red color and called heart failure cells

Surfactant

- Surface tension reducing agent.
- Synthesis starts at 20 wks & peaks at 35 weeks in a fetus.
- Surfactant is secreted by Type-II pneumocytes (granular cells). Number of inclusions and size of type-II pneumocytes is \uparrow ed by Thyroid hormone maturation and glucocorticoids.
Maternal DM (= fetal hyperinsulinemia), high insulin and smoking \downarrow surfactant synthesis, high incidence of HMD/ RDS
- It is a mixture of **phospholipids** (mainly dipalmitoyl phosphatidyl choline (DPPC) 62%), other lipids, proteins & CBH.
- **Funcⁿ**—It \downarrow es alveolar surface tension thus \uparrow es compliance (prevents alveolar collapse/atelectasis), prevents pulmonary edema (transudation of fluids from blood into alveoli). It \uparrow es the radius of alveoli & compliance of lung
- **Deficiency may occur with** --- Occlusion of pulmonary a., occlusion of main bronchus, smokers, prolonged 100% O₂ therapy
- **Deficiency leads to** --- HMD in preterm newborns (FRC is below the closing volume, CPAP is required to \uparrow FRC to a level above CV so that terminal airways remain open throughout the cycle)

Normal Arterial and Venous Blood Parameter

Parameter	Arterial blood	Mixed venous blood
O ₂ tension PaO ₂	95 mmHg	40 mm Hg
O ₂ saturation of Hb	0.98	0.73
Hb bound O ₂	197 mL/L	147 mL/L
Dissolved O ₂	2.7 mL/L	1.2 mL/L
Total O ₂ content	200 mL/L	148 mL/L
Blood volume	1.25 L	3.75 L
Volume of O ₂	250 mL	555 mL

Alveolar - arterial O_2 difference (A-a O_2 Diff.)

Normal in

High altitude (hypoxemia with PaO_2), Hypoventilation

A-a O_2 Diff is High [PaO_2 is low]

ILD's (Defective oxygenation, V/Q mismatch (pneumonia, ARDS L→R Shunt)

↑↑ Shunting (Rt. → Lt.) (pneumonia, ARDS, atelectasis, Diffusion abnormalities)

Defect in ventilation (e.g. in obstruction as in COPD, asthma, pulmonary edema & in **hypoventilation** as in CNS depression, respiratory m/s fatigue) COPD.

OXYGEN THERAPY

Role of 100% Oxygen

- Administration of 100% O_2 ↑es the O_2 content of alveolar air and improves the hypoxia d/to fibrosis, hypoventilation, impaired diffusion or V/Q mismatch by ↑ing the amount of O_2 leaving the lungs.
- 100% O_2 is NOT effective in tetology of Fallot.

Oxygen toxicity

- O_2 content in tissue beyond certain critical level (>2 atmosphere) is called O_2 toxicity
- Seems to be d/to the superoxide anion (O_2^- which is a free radical) and H_2O_2
- Leads to tracheobronchial irritation & pulmonary edema (first change), tissue burn out, hyperirritability of CNS

Hyperbaric oxygen (HBO)

- HBO mainly increases dissolved O_2
- Administration of pure O_2 (HBO) is dangerous as it leads to

apnea d/to hypostimulation of peripheral chemoreceptors.

→ O_2 therapy is most useful in --- hypoxic hypoxia

→ HBO is useful in CO poisoning, surgery for certain CHD, in t/t of gas gangrene, CO poisoning, and probably cyanide poisoning. However, O_2 toxicity limits exposures to < 5 hours and pressures to ≤ 3 atm.

→ Arterial O_2 content is ↓ in --- Anemic hypoxia (normal in--- stagnant and histotoxic hypoxia)

→ Peripheral chemoreceptors are not stimulated in --- Anemic hypoxia (CO poisoning, anemia)

→ PCR have very high rate of blood flow (2L/min) so stimulate PCR when stagnation.

→ Baroreceptors are most sensitive to --- rise in SBP

→ Acute hypoxia at high altitude is d/to --- Stimulation of chemoreceptors

→ O_2 therapy is not useful in --- histotoxic hypoxia

HYPOXIA

Hypoxic hypoxia (Hypoxemia)

Is d/to high altitude, impaired ventilation d/to any cause, central depression by analgesics, neuromuscular palsy, lung d/s. In Rt. to Lt. shunts chronic hypoxic hypoxia + cyanotic CHD result.

Anemic hypoxia ---- CO poisoning, anemia

CO forms COHb which can not take up O_2 . The affinity of Hb to bind CO is 210 times its affinity for O_2 . COHb liberates CO very slowly.

Types	Single best test	P_AO_2	PaO_2 (O_2 tension or dissolved O_2)	O_2 content (O_2 carrying capacity)	A-V O_2 difference	% saturat ⁿ SAO_2	Stimula ⁿ of PCR	Other/ Remark
Hypoxic	PaO_2	↓	↓↓	↓	N	↓	+	↑ 2,3 DPG, O_2 therapy useful
Anemic	O_2 content (or Hb%)	N	N	↓↓	N	↓↓	-	↑ 2,3 DPG, shift to right, hyperkinetic circula ⁿ , ↑ turbulence
Stagnant	A-V O_2 difference	N	N	N	↑↑	N	+	
Histotoxic	A-V O_2 difference or PO_2 venous blood	N	N	N	↓ or 0	N	+	<u>Venous blood is bright red.</u> A-V difference of O_2 is nil or very low (tissue can't extract O_2 from arterial bld)

[P_AO_2 = Partial pressure of Alveolar oxygen, PaO_2 (O_2 tension) = Partial pressure of arterial oxygen, SAO_2 = Oxygen saturation,

A-V O₂ diff = Arterio venous oxygen difference, N = Normal,
PCR = Peripheral chemo receptor]

Stagnant hypoxia

Seen in cardiac /circulatory failure, severe shock, h'age etc. ↓
capillary blood flow

Histotoxic hypoxia

Defect in tissue oxygenation. E.g. cyanide poisoning, overdose
of anesthetic/narcotic drugs, which can directly stimulate PCR.

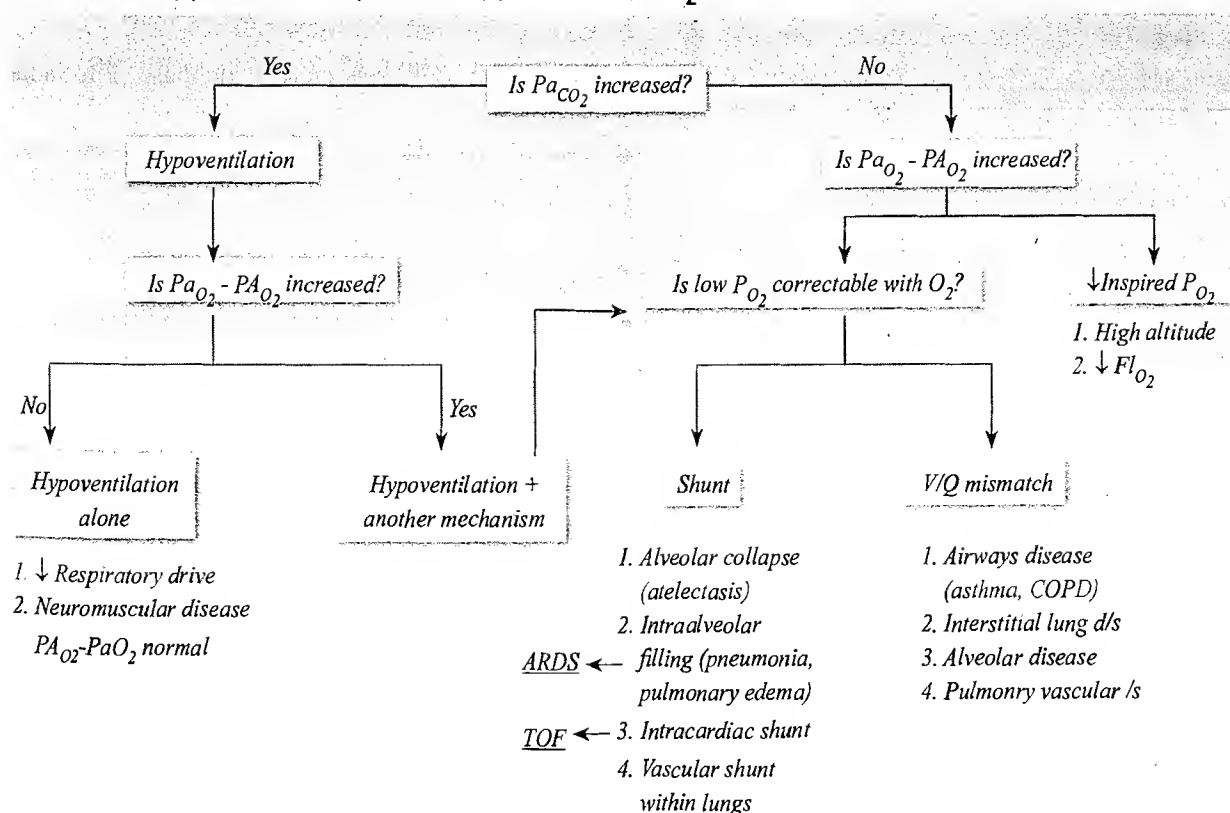
Peripheral Chemoreceptors (PCR)

- Cyanide (histotoxic hypoxia) can directly stimulate PCR.
- If PCR is removed hypoxic drive will be lost completely.
becoz PCO₂ stimulates only PCR.
- PCR have very high rate of blood flow (almost 2000mL/
min.). So stimulate PCR whenever there is stagnation.
- Carotid bodies are susceptible only to dissolved O₂ or O₂
tension (P_aO₂ values) and not to the O₂ content. As P_aO₂
is normal in anemic hypoxia, PCR are not stimulated and
there is no dyspnea at rest. However, dyspnea is quick to
appear on exertion.

DEAD SPACE

- Total dead space = Anatomical DS + Alveolar DS
- *Anatomical DS* : It is the volume of air present in
"conducting zone" of respiratory passage i.e. nose,
trachea, upto terminal bronchioles, where exchange
of gases does not take place. Normally it is 30% of
tidal volume or 2ml/kg or ~150 ml. Anatomical DS is
measured by **single breath N₂**.
- DS is ↑ in : Old age, extension of neck, protrusion of jaw,
bronchodilation, atropine, anaesthetic mask/circuits, long
ETT, IPPV, PEEP, ↑ lung volume.
- DS is ↓ in : Hyperventilation, neck flexion, intubation,
brocho-constriction, tracheostomy.
- *Alveolar DS* :
Constituted by alveoli which are only ventilated but not
perfused. It is 60-80 ml in standing & 0 in lying down
position. It is ↑ by any lung pathology affecting diffusion
at alveolar capillary membrane like-ILD, PE, ARDs, GA,
IPPV and PEEP, hypotension, emphysema, bronchiectasis.
Alveolar DS is measured by Bohr's equation

Diagnostic approach to a pt with hypoxemia (PaO₂ < 80 mm Hg)



Blood gases and Properties of gases

Transport of Oxygen in blood

- Oxygen is transported in blood mainly (97%) in chemical combination with Hb (in form of **oxyhemoglobin**)
- Only 3% oxygen is transported in dissolved state in plasma.
- Arterial blood contains 19 mL O₂ /100 mL of blood.

Transport of CO₂ in blood

- CO₂ is transported in blood mainly (70 %) in the form of **bicarbonates**
Plasma HCO₃⁻ > carbamino compounds > dissolved CO₂ plasma
- CO₂ is 20 times more soluble in blood than oxygen & its dissociation curve is linear over physiological range.

Properties of gases

- N₂O is perfusion (flow) limited gas
- Carbon monoxide (CO) is a diffusion limited gas. So DL_{CO} is used as an index of diffusing capacity.

- Diffusion capacity is measured by formula $D_{LCO} = \frac{V_{CO}}{P_{ACO}}$

Properties	O ₂	CO ₂	CO
○ Affinity ratio	1	20	200
○ Diffusion capacity	1	20	1
○ Solubility	1	24	

- CO₂ can diffuse more easily than O₂ becoz solubility of CO₂ is 24 times more in plasma (liquid phase) than that of oxygen

Blood gas content

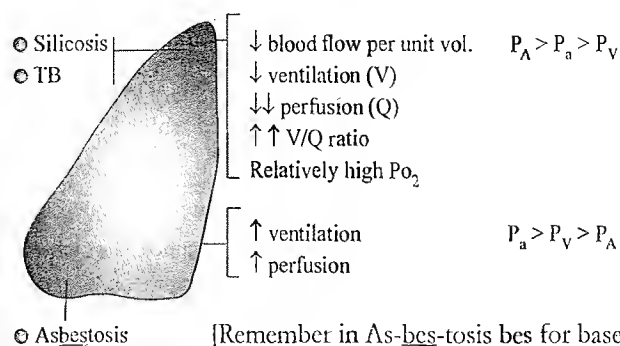
- Amount of oxygen dissolved in blood can be derived from Henry's Law.
Henry's Law states that the concentration of any gas in solution is proportional to its partial pressure.
Gas Concentration = α X partial pressure
- Total O₂ content of arterial blood is 200 mL/L while that of mixed venous blood is 148 mL/L

$$\text{O}_2 \text{ content} = \text{dissolved oxygen in plasma} + \text{O}_2 \text{ contained in the Hb}$$

- Mouth to mouth respiration provides 16% of O₂.
- O₂ content of inspired air is 21%, alveolar air is 14%, and that of expired air is 16%
- Room air or atmospheric air contain 78% N₂ + 21% O₂ + 1% other gases

Ventilation Perfusion Gradient in Standing

- In the upright position, ventilation(V), perfusion(Q), & intrapleural pressure all decline from the bases to apex. However V/Q ratios ↑ from base to apex. Relatively high PO₂ favors growth of mycobacteria and TB at apex.



- Alveolus at the base is less expanded compared (see diagram) to apex d/to less negativity, hence c/b more ventilated. Intrapleural pressure is -2.5 cm of H₂O at base & at apex it is -10 cm of H₂O.
- Alveolar O₂ (P_AO₂) is more at the base d/to more ventilation.
- Arterial O₂ (P_aO₂) is maximum at apex d/to more V/Q ratio. TB is common.

Oxygen Hb Dissociation Curve (ODC)

- ODC is the curve drawn after plotting the partial pressure of oxygen (PaO₂) on X-axis and % saturation of hemoglobin (Hb%) on Y-axis.
- It is sigmoid shaped curve d/to **positive co-operativity** (Every molecule of Hb got 4 haeme, each binding ↑ es the affinity for other)
- Shifts to right favours delivery of O₂.
- Shifts to left favours affinity of O₂.
- **Bohr effect:** The binding of CO₂ to Hb in the tissues augments delivery (unloading) of oxygen from capillary blood. Hb easily releases O₂ when the pH decreases because of ↓ in O₂ affinity.
- **Haldane effect:** Binding of oxygen to Hb in the alveolar

capillary bed augments CO_2 unloading from capillary blood into the alveoli. The reduced Hb holds more CO_2 than the oxygenated blood at same P_{CO_2} .

● **Hamburger effect (Cl^- shift):** Process refers to the exchange of bicarbonate (HCO_3^-) and chloride (Cl^-) across the membrane of red blood cells.

- ODC is sigmoid shaped which plateaus off at $\text{PO}_2 > 70 \text{ mm Hg}$. Thus a patient with very high PO_2 may have a saturation 97-99%.
- Pulse oxymetry does not measure the PaO_2 and thus relatively insensitive in detecting hyperoxemia.
- Normal oxygen saturation is 95-98%.
- Hb-F had higher affinity of O_2 because of ↓ 2,3 DPG.
- CO poisoning : CO has very high affinity for Hb. It displaces O_2 & combines with heme. % Saturation is ↓. It ↑ the affinity of heme with O_2 .
- In a patient of hemorrhage it is better to give fresh blood not the banked blood because O_2 delivery will be less d/to shift of ODC to left.
- Hypoxemia does NOT depend upon ---Hb.
- CO_2 is 20 times more soluble in blood than oxygen and its dissociation curve is linear over physiological range.
- ODC is normal in diabetic ketoacidosis (but anion gap is ↑).

Shift of ODC

Shifts to left	Shifts to right
↓ Temperature	↑ Temp
↓ H^+ or ↑ pH (alkalosis)	↓ pH, ↑ H^+ (acidosis)
↓ 2, 3 DPG	↑ 2, 3 DPG
↓ PCO_2	↑ PCO_2 , hypoxia
↑ HbF, Myoglobin (Mb)	↑ Hb-S
CO-poisoning	High altitude

[All ↑ in Rt shift except pH & O_2]

2,3-Biphosphoglycerate [BPG] or 2,3 DPG

- Present in high concentration in RBCs
- A low PO_2 in peripheral tissues (hypoxia) promotes the synthesis of 2,3- BPG in erythrocytes in glycolysis.
- BPG stabilizes deoxygenated (T-state) Hb by forming salt bridges. It greatly reduces the affinity of Hb to O_2



Promotes delivery (unloading or release) of O_2 .

- It does not combine with fetal Hb.
- 2,3 DPG ↓ es in stored blood. Use of CPD-A as preservative causes less ↓ in 2,3 DPG.

● **Factors affecting RBC 2,3 DPG concentration :**

↓ in 2, 3 DPG	↑ in 2, 3 DPG
Transfusion with banked blood → left shift	Growth hormone
Acidosis (H^+)	Exercise
	Thyroid hormone
	Anemia, androgens, high altitude
	[Mnemonic : GETA]

Nitrogen Narcosis

- Seen in sea divers who go below 100 feet in sea.
- Effect of N_2 gas on brain d/to law of partial pressure.
- Pressures are very high (~ 2 atmosphere at 33 feet and 3 atmosphere at 66 feet). Air is supplied at very high pressures to prevent lungs from collapsing (Hyperbarism). N_2 dissolves fatty substances in neuronal membranes & ↓ es excitability.

CO_2 Narcosis

- Seen in COPD patients or when people are given too much oxygen..This slows down the oxygen driven drive to breathe.

Decompression Sickness/Caisson's d/s

- Also k/as Bends, Diver's paralysis, Dysbarism.
- Form of gas embolism (formation of obstructive gas bubbles) d/to sudden lowering of atmospheric pressure.
- Seen in deep sea divers, rapid ascent of scuba, unpressurized aircraft in rapid ascent.
- Gas bubbles within skeletal system is responsible for bends.. Chokes occur in lungs.

Changes seen in acclimatization to high altitude

A height >10, 000 feet (3000 meters) above sea level is considered high altitude. At high altitude barometric pressure ↓ es and there is ↓ in p_{O_2} and ↓ in p_{N_2} while p_{CO_2} and $p_{\text{H}_2\text{O}}$ remain constant. In an acclimatized individual O_2 delivery to tissues is maintained by hemoconcentration.

- ↑ 2, 3 DPG of RBCs (↓ affinity of O_2 for Hb), ↑ in P_{50}
- ↑ Erythropoietin secretion --- polycythemia vera (↑ RBC volume or Hct), red cheeks

- ↑ no. of mitochondria & tissue content of cytochrome oxidase, ↑ pulmonary ventilation.
- ↑ in myoglobin
- Barrel shaped chest,
- Alkaline urine is produced.

→ If high hematocrit (~ 60) is found in a mountaineer it indicates polycythemia + dehydration.

→ Critical survival altitude is 25000-30,000 feet, above this level oxygen therapy is required.

Effect of acceleration or positive 'g'

- ↓ CBF, ICT and cardiac output
- **Blackouts**/ unconsciousness may be seen on acceleration >5 'g'

Effect of deceleration or negative 'g'

- ↑ Cardiac output, cerebral arterial pressure, and CBF
- **Redouts** (throbbing headache, confusion, echymoses etc)

Brainstem/Neural Respiratory Centres

Centre	Location	Function
DRG	Dorsomedial region of medulla	Stimulation of respiration
VRG	Nu ambiguus rostrally, Nu retroambiguus caudally	Remains inactive during quiet/ normal respiration, ↑ expiration during exercise
Pre BOTC	Located on either side of medulla. Contain pacemaker cells.	Discharges automatically causing inspiration by phrenic nerve stimulation
Pneumotaxis centre	Dorsally in the nu. parabrachialis of the upper pons	↑TRR by ↓ing inspiratory time

→ Centre for automatic (spontaneous rhythmic) respiration control is Pre- Botintzer complex (pre-BOTC). So Pre BOTC is also k/as pacemaker of respiration.

→ Apneustic centre is located in ---Lower pons. It regulates depth of breathing.

→ Depth of inspiration is increased after vagotomy.

Transection of brain-stem levels & respiration

Transection level in brainstem	Result
• Inferior colliculus (rostral to pons)	--- Normal automatic respiration
• Mid pons	--- Apneusis (prolonged inspiratory spasm)
Damage to pneumotaxis centre + both vagi cut.	
• Below medulla	--- No breathing, Respiration stops

Abnormal Respiratory Patterns

Breathing	Pattern	Seen in
Chyne stokes respiration	Periodic, apnea--hyperapnea	Uremia (CRF), Opiates poisoning, CCF, hypoxia
Biot's	Periodic breathing irregularly irregular	Meningitis
Kussmaul's	Rapid and deep breathing (air hunger)	Metabolic acidosis (DKA, Uremia)
Agonal gasps	Terminal respiratory pattern	Lower brainstem/ medullary damage
Ondine's curse	Loss of automatic respiration	

Non-respiratory functions of lung

- Sodium exchange
- Change in pCO₂
- Filtration of micro-clotts in veins.
- Filter out micro-bubbles of gases.
- To convert angiotensin I → Angiotensin II

GIT AND LIVER

Appetite

Appetite stimulants (Orexigenic peptides)	Appetite suppressants (Anti-orexigenic peptides)
Orexins A and B, b- endorphins, endocannabinoids	Serotonin
AGRP (Agouti related peptide)	CART
GALP	GLP, GRP, Glucagon
MCH	α MSH
NPY	CGRP
GnRH (Gn releasing hormone)	CRH (Corticotrophin releasing hormone)

- **Neuropeptide Y (NPY)** is a polypeptide containing 36 amino acids. It acts as a neurotransmitter in brain and ANS. Secreted by hypothalamus. It is involved in ↑ in appetite. In starvation its levels are increased along with melanocorticotropin (MCH), they generate heat (calories).
- **Ghrelin** is a polypeptide GI hormone secreted from stomach (P/D₁ cells lining the fundus) and hypothalamus. It is involved in control of food intake by GH stimulating activity. It stimulates appetite, its secretion is increased by fasting/ starvation.

Absorption

- Proximal intestine is the site of absorption of: Iron, calcium, water soluble vitamins (B & C), fat (long chain FA)
- Proximal and mid intestine: Sugars
- Middle small intestine / Jejunum: Amino acids.
- Distal SI (terminal ileum): Bile salt & Vit. B12
- Colon (esp. caecum): Secretes mucous and absorbs water, electrolytes and short chain FA.

Absorption from GIT

- **Rate of absorption from GIT**
Galactose (max^m) > Glucose > Fructose > Mannose
- Glucose is reabsorbed maximally. Absorption of Glucose is ↑ed from intestine by - Thyroid hormone, ant. pituitary hormone, ACTH, Vit. B₁, B₆ and Pantothenic A. Insulin has no effect on absorption of glucose in GIT.

Absorption of iron

- Occurs from SI (duodenum & upper jejunum) in the Ferrous (Fe²⁺) form.
- Bioavailability of iron (absorption) is best in heme form
Heme > Fe²⁺ > Fe³⁺

Effect	Example
Physical state	Heme > Fe ²⁺ > Fe ³⁺
Facilitators	Ascorbate (vitamin C), citrate, amino acids, Iron deficiency
Competitors	Lead, cobalt, strontium, manganese, zinc
Inhibitors	Phytates, tannins, soil clay, laundry starch, iron overload, antacids

Absorption of Calcium

- Occurs from SI (jejunum).

- Active transport across GI mucosa is favored by 1,25 (OH)₂ D, the active form of vitamin D.

- Iron is absorbed from — Duodenum and proximal jejunum
- Calcium, folate from — Jejunum
- Vit. B₁₂ & Bile salt — Terminal ileum.

Composition and secretion of gastrointestinal juices and saliva

Juice	Daily secretion (in Litre)	pH	Rich in	Major enzymes
Saliva	1.5	6.9	K, Na ⁺	Ptyalin, lipase (no proteolytic enzyme)
Gastric	3	1-2	Na ⁺ , H ⁺	Pepsinogen (no saccharolytic enzyme)
SI juice	3	7.6	Na ⁺	SI enzymes
Pancreatic	1.2-1.5	7.8-8.4	Na ⁺ , H ⁺	Trypsinogen, peptidases (Alkaline with high pH)
Hepatic bile	0.5-1	7.8-8.6	Na ⁺ , HCO ₃ ⁻	Rich in water & HCO ₃ ⁻
GB bile	0.5-1	7.0-7.4	K ⁺	Rich in bile salts

- Mucin secreting cells/glands of GIT are — Goblet cells, Brunner's glands (duodenum), and Crypts of Lieberkuhn
- Most alkaline secretions: Brunner's gland secretion (pH 8-8.9) > hepatic bile (pH 7.8- 8.6) > pancreatic juice
- K⁺ concentration is max^m in Saliva > colonic fluid/rectal fluid
- Max^m water reabsorption occurs in jejunum.
- Max^m fluid & nutritional consequences are seen after resection of ileum.
- No proteolytic enzyme is present in mouth
- No saccharolytic (CBH splitting) enzyme is found in gastric juice.

Cells/glands of stomach and intestine

Location	Cell type	Function / Secretion
Fundus (cardia)	Chief cells/ zymogen cells	Pepsinogen, blood group substance
Neck	Parietal cell or oxyntic cell	Secretes HCl + Intrinsic factor of Castle
Isthmus	Mucous cells	Mucin + HCO_3^-
Pylorus/antrum	G-cells, D-cells	Gastrin, Somatostatin
Duodenum	Brunner's gland	Mucus
Small intestine	Paneth cells (in Crypts of Lieberkuhn)	Guanylin (Role in mucosal immunity)
Mucosa of SI	Enterochromaffin cells	Serotonin
Intestine	Goblet cells	Mucus

→ Chief cells are most abundant in fundus of stomach.

→ Acid secretory stimuli in stomach - Ach, gastrin, insulin, alcohol, food hunger, histamine (H_2).

→ Gastric acid secretion is ↓ed by — Glucagon, anti-histaminics.

→ Gastrin promotes gastric emptying by ↑ing small bowel motility.

→ Oral calcium carbonate ↑sed serum gastrin and gastric acid output.

Regulation of Gastric secretion

1. Cephalic phase : Mediated by cholinergic/vagal mechanisms (Parasympathetic)
2. Gastric phase: local, stretch reflex (chemical effects of food and distension of the stomach).
3. Intestinal phase: Probably neuro hormonal (Gastrin)

Gastrin

- Released in response to - stomach distension, vagal stimulation (mediated by the neurocrine bombesin, or GRP in humans), the presence of partially digested proteins especially amino acids and hypercalcemia.
- Release is inhibited by: The presence of secreted HCl/acid in the stomach (a case of negative feedback); Somatostatin, secretin, GIP (gastroinhibitory peptide), VIP (vasoactive intestinal peptide), glucagon and calcitonin.

Gastric emptying

- Stimulated by: Gastrin, excitement, carbohydrate rich food.
- Delayed by: Fatty meal (causes slowest emptying), protein rich food, acid bathing & distension of duodenum by stimulating enterogastric reflex (neurally mediated), GIP, enterogastrones (CCK + secretin). Hormones that inhibit emptying include cholecystokinin, secretin, and Gastric Inhibitory Peptide (GIP). Secretin is secreted in response to acidity in the duodenum, Cholecystokinin and GIP in response to the presence of fats in the chyme.

Gastric motility

- ↑ by: Gastrin, histamine, Ach, nicotine, K^+
- ↓ by: enterogastrones (CCK + secretin), epinephrine, norepinephrine, atropine, Ca^{++}

Small bowel motility & effect of GI hormones

- ↑ by: Gastrin, CCK, substance P, neurotensin, PPP, motilin.
 - ↓ by: Secretin, glucagon, Peptide YY, VIP
- Intestinal motility depends upon gastric motility. Wave of depolarisation starts from stomach and peristaltic wave is generated caudally towards ileus k/as MMC. In the small bowel, the **cleansing** action of antegrade peristalsis (grooming and cleansing of bowel), especially the migratory motor complex (MMC), is responsible for sweeping bacteria into the colon.
- Pepsinogen:** is activated by auto activation (pH-2) or Autocatalysis.
 - Max^m post prandial motility is seen in descending colon.
 - After paralytic (adynamic) ileus intestinal peristalsis returns in 6-8 hours (earliest) followed by gastric peristalsis, but colonic activity takes 2-3 days to return.

Segmental contractions

Used to churn & mix the food with the digestive juices or chyme & it brings the chyme into contact with the epithelial cells for absorption. The circular muscles in adjacent segments of the intestine undergo alternate contraction and relaxation.

Peristaltic contractions

Move or propel food and chyme down the lumen of the bowel. **Circular muscles** contract behind a bolus of food, the muscles in front of the bolus relax and this wave of contraction proceeds down the bowel propelling the bolus of food forward. Gastrin, CCK & motilin stimulate muscle contractions (peristalsis), whereas muscle activity is inhibited by secretin and often by glucagon.

Bile

- Secreted by hepatocytes into the bile capillaries and from there into duodenum through "Sphincter of Oddi"
- Bile is concentrated and stored in GB. When food enters the duodenum, secretin & CCK-PZ stimulate GB to contract & bile is poured into the duodenum.
- Choleretics** are the substances that \uparrow bile secretion. Bile salts are most potent choleretics.
- Cholagogues** are the substances that \uparrow GB contraction e.g. Fatty acids & amino acids in duodenum release CCK, Ca^{++} ions.
- Rate of bile production is 500 ml/d and that of bile salts is 0.2-0.4 gm/d. Substance which \uparrow bile production — Vagus stimulation, secretin ($\uparrow \text{HCO}_3^-$ & water content of bile).

Bile acids

- Principle/Primary Bile Acids :**
Formed in liver from cholesterol
 - Cholic acid
 - Chenodeoxycholic acid
- Secondary bile acids :**
Formed in the colon by bacterial action. Primary bile acids are converted into 2° bile acids which are
 - Deoxycholic acid &
 - Lithocholic acid respectively.

Bile salts

- Are sodium or potassium salts of bile acid conjugated with glycine or taurine. e.g. Na^+ -Glyco/tauro-cholate or K^+ -Glyco/taurocholate. Taurine is synthesized by cysteine/sulfinic acid pathway in pancreas.
- They \downarrow se surface tension and responsible for emulsification of fat along with phospholipid and monoglycerides.
- Bile salts are amphipathic
- $\uparrow \downarrow$ Bile salts excretion in urine is seen in obstructive jaundice.

GB-bile	Hepatic bile
Rich in K^+	Rich in $\text{Na}^+ \text{HCO}_3^-$
pH 7.0-7.4	pH 7.8-8.6
(Acidic)	(Alkaline)

Pancreatic secretions

- Pancreatic secretions are mainly under hormonal control. Secretin & CCK-PZ are major hormones.

Features	Secretin	CCK-PZ
Stimulus	Acidic gastric juice	Fatty meal in chyme > peptones, vagal
Secreted by	S-cells in mucosa of duodenum	mucosa of jejunum
Effect	Watery & alkaline pancreatic juice rich in HCO_3^-	Contraction of GB \downarrow Pancreatic juice rich in enzymes

→ Secretin is homologous to glucagon

→ Secretin augments the contraction of pyloric sphincter along with CCK

- Islet of Langerhans is endocrine part. It contains 3 types of cells which secrete different hormones.

Cells	Secretion	Role
α	Glucagon	Gluconeogenesis, \uparrow sugar
β	Insulin	Inhibit secretion of glucagon
	Amylin	Inhibits secretion of insulin
δ	Somatostatin	Inhibits secretion of insulin & glucagon

JAUNDICE

- Jaundice is visible in sclera if total s. bilirubin is $> 2.5 \text{ gm\%}$
- M/c cause of jaundice in a newborn in first 24 hr → ABO incompatibility
- M/c cause of dark coloured urine with acholic (clay coloured) stools → obstructive liver d/s
- Gilbert syndrome** → M/c genetic cause of jaundice Unconj. hyperbilirubinemia d/to \downarrow UGT activity.
- Crigler Najjar syndrome** → AR defect a/w unconj. hyperbilirubinemia. Two types are there : CN1 & CN2
- UGT (*Uridyl Glucoronyl Transferase*) Defects

Feature	CN1	CN2	Gilbert's
Mode	AR	AR	AR + AD
UGT activity	0%	10%	33%
Histo	N	N	Lipofuscin/black pigment
Kernicterus	Common	Rare	Never
Mortality	<1 yr	Adulthood	Not \uparrow

● Isolated conjugated hyperbilirubinemia

Feature	DJS (Dubin Johnson)	Rotor's
● Defect	Mutation of MRP-2 protein	Defective transport
● Effect	Defective canalicular excret ⁿ	-
● Histo	Black pigment d/to metabolites of epinephrine	N

[Mnemonic : DR. are conjugated]

● 3 Major categories of jaundice

	Hemolytic	Hepato-cellular	Obstructive
● Type of ↑ in bilirubin	unconjugated	Conjugated	Conjugated
● Urine :	(acholuric)		
- Colour	Turneric		
- Urobilinogen	+++ (turns dark on standing)	++	-
- Bilirubin	-	+	++ (Bilirubinuria)
● Stool			
- Colour	N	N (in early phase)	Clay coloured
- Sterco-bilinogen	+	+	
● Vanden Bergh's reaction	Indirect	Direct/ Indirect	Direct

KIDNEY AND URINARY TRACT

Anatomical and Physiological consideration

- **Cortical nephrons** (short loop neurons) are found in cortex. They constitute 85% of all neurons
- **Juxtamedullary nephrons** extend in medulla as they have long loops. They constitute 15% of all neurons. Maximum no. of J~ are found in camels so water conserving mechanism is well developed

● Glomerular Filtration Barrier:

Has fenestrations of 70-100 nm range. It is formed by Endothelial cells + Podocytes (visceral epithelial cells) + GBM (Proteoglycan) -ve charge on both surfaces.

● Juxtaglomerular Apparatus(JGA):

Formed by JG-cell + Lacis cell + Macula Densa

Part	JG-cell	Lacis cell	Macula Densa
Location	afferent arteriole	In junction b/w aff. & efferent (in mesangium)	In distal tubule (at the junction where aff. arteriole enters & eff. arteriole leaves)
Function	Secretes renin	Contains renin	Senses the change in NaCl conc ⁿ

→ When Na^+ load is low in DCT JG-cell of JGA increased and secretes renin.

Tubular System

- Glomerular membrane permits free passage of neutral substances upto 4 nm in diameter (>8 nm size totally excluded). Filtration pressure of renal glomeruli is 15 mmHg.
- Total length of nephron = 45 – 65 mm
- Proximal tubule (PCT) reabsorbs almost 100% of glucose and urea, ~ 80-90% of HCO_3^- , 65% of water, 60% of Na^+
- Reabsorption of water is obligatory to Na^+ reabsorption. It is coupled with Na^+ reabsorption in renal tubules.

→ Thin & thick ascending limb of LOH, early distal tubules are impermeable to water

→ > 50% potassium that appears in urine is derived from secretion by distal tubule

→ Osmolality of urine depends upon — action of vasopressin on collecting ducts

→ Acidification of tubular fluid (urine) occurs in collecting ducts

→ Reabsorption of glucose is coupled with Na^+ reabsorption in GIT k/as Glucose- Na^+ symport which is the basis of use of ORS in diarrhea

→ Kidney secretes 3 important hormones — Renin, erythropoietin, and vitamin D_3

PCT		LOH			CD
		DL	Thin AL	Thick AL	
Length	15 mm	5 mm			20 mm
Epithelium	Cuboidal epithelium with multiple microvilli and brush border cells	Flat	cuboidal	cuboidal	Columnar
Function					Acidifica ⁿ of urine
Permeability					
- Max ^m for	Water				
- Reabsorp ⁿ	HCO ₃ ⁻ , Na ⁺ , K ⁺ , IP, glucose, urea, aa		Na ⁺ (passive), Cl ⁻	Na ⁺ , Cl ⁻	Na ⁺ uptake
- Permeability to water	++++	++++ (Max ^m)	Impermeable	Impermeable	
Remarks	Excretion (not absorption) of H ⁺ ions	Na ⁺ is not reabsorbed in this part		Cl ⁻ is completely reabsorbed	

Assessment of renal functions

Renal function	Standard method to measure	Other tests to measure it
GFR	Inulin	U, Cr clearance, DTPA etc.
RPF (Renal plasma flow)	PAH test	
RBF (Renal blood flow)	RPF x [1/ (1-hct)]	
Tubular function	Sp gravity	15 min PSP excretion test

GFR

- Formula to calculate GFR

$$\text{GFR} \propto \text{EFP} [\text{EFP} = P_g - (P_B + \text{COT})]$$

$$\text{GFR} \propto K_F \cdot \text{FF}$$

\propto Permeability of filtering membrane

P_g = Glomerular capillary pressure (\uparrow BP $\rightarrow \uparrow P_g$)

P_B = Pressure in Bowman's capsule (Hydrostatic P.)

COT = Colloidal osmotic tension of plasma in glomerular capillaries

- In case of hypotension GFR is maintained by constriction of eff. arteriole.
 \downarrow in BP and \downarrow in GFR $\rightarrow \downarrow$ in renal blood flow in aff. arteriole \rightarrow Constriction of eff. arteriole \rightarrow maintain GFR.
- GFR \uparrow es if afferent arteriole dilates.
- GFR is measured by **inulin clearance**. Inulin is the standard substance to measure GFR becoz it is filtered but not reabsorbed. Urea clearance, Creatinine clearance, DTPA are other substances to measure GFR.

- GFR in a normal resting person is 125ml/min or 180 L/d, whereas the normal urine volume in 24 hours is approximately 1L/d (or >1 mL/kg/hr). Thus 99% of glomerular filtrate is reabsorbed.

- Factors affecting GFR :

Prostaglandins \uparrow GFR

Diarrhoea, fluid loss \downarrow GFR

- Substance which is not normally filtered/reabsorbed to significant degree by renal tubules: Xylose
- Creatinine clearance is best test for measuring glomerular function
- The main function of renal tubules is concentration of urine & it can be measured by specific gravity of urine

- Renal plasma clearance of various substances :

$$P_{\text{PAH}} > C_{\text{Cr}} > C_{\text{inulin}} > C_{\text{glu}}$$

For glucose it is 0 i.e. nil.

Renal threshold

Plasma level of glucose at which glucose first appears in urine 180 mg% (venous) or 200 mg% (Arterial) blood glucose.

- Transport maximum of Glucose (T_m) — 360 mg/min (Splay phenomena is seen)
- In renal glycosuria renal threshold for glucose is low
- Urea have no T_m (Tubular maximum) value.
- Maximum urine acidity 0.03, normal urinary pH = 5.85, specific gravity 1.015-1.025
- Daily loss of N₂ in urine 20-50 gm.

Micturition and emptying of bladder

Bladder Volume	Effect
100 mL	Residual volume of urine in bladder. Bladder emptying is not possible
150 mL	First urge to void is felt
300-400 mL	Marked sense of bladder fullness is felt & voiding occurs

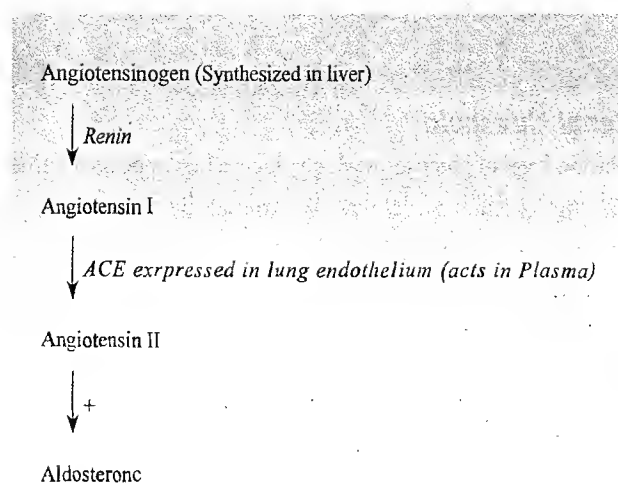
- Detrusor m/s increase the pressure in bladder upto 40-60 mmHg → Emptying of bladder.
- Higher centre for bladder continence and M~ is located in paracentral lobule of frontal lobe.

Counter Current Multiplier System

- Responsible for **medullary hyperosmolality** of interstitial fluid (d/to increased interstitial Na^+ , K^+ & urea) & medullary gradient
- Prime driving force for counter current multiplier mechanism is *reabsorption of Na^+* in thick ascending limb
- When there is negative water balance (contraction of ECF volume) or water deficit in the body urinary concentrating ability of kidneys is increased to conserve water and urine is produced with small volume.

Renin angiotensin aldosterone axis

- In response to renal ischemia, renin is secreted from JGA and it converts angiotensinogen to angiotensin I
- Angiotensin I is converted into Angiotensin II by the action of converting enzyme present in plasma. Angiotensin II stimulates adrenal cortex to secrete aldosterone which retains water and electrolytes (Na^+)



Renin

- Renin is an acid protease enzyme secreted by **DCT** of kidney. It converts angiotensinogen to angiotensin I
- Tubuloglomerular feed back is a feedback from renal tubules to regulate GFR
- Macula densa is the sensor for its secretion. *When Na^+ load is low in Macula densa* of DCT, JG cell of juxtaglomerular apparatus are stimulated and secretes renin

Erythropoietin

- Circulating glycoprotein secreted by mesangial cells of glomeruli of JGA of **kidney (85%)**. In fetus it is produced by liver /cells of monocyte/macrophage lineage.
- Principal site of inactivation is liver ($t_{1/2}$ is 1 hr.), peritubular capillary of renal cortex.
- **Blood level is ↑ed in hypoxia** (physiological stimulus) & anemia. Secretion of E~ is ↑ed by Cobalt, androgens, high altitude, alkalosis, adenosine, catechol amines & ↓ed by adenosine antagonist theophylline.
- *It does not cross placenta therefore stimulation of maternal EPO does not result in stimulation of fetal RBC production.*

Site of action of some imp. Hormones

Hormone	Stimulus	Secreted from, site of action	Action
Angiotensin II	↓ BP	P cells of Cortical CD & DT	Constriction of afferent arteriole. ↓ GFR
Aldosterone		Zona glomerulosa of the adrenal cortex	Retention of Na^+ Excretion of K^+ → M/s fatigue, expansion of ECF volume
ADH (Vasopressin)	Low pressure in atria	Medullary CD & DT	Water retention
ANP		RA of heart	Promotes natriuresis

[CD = collecting ducts, DT = Distal tubules]

- Osmolality of urine depends on the action of vasopressin on the collecting ducts.
- There are 3 type of vasopressin receptors :

Type	Site	Action
V_{1A}	Vascular SM Brain Liver	Vasoconstriction ↓ cardiac output ↑ glycogenesis
V_{1B} or V_3	Anterior pituitary	↑ ACTH
V_2	CD	↑ water diffusion through aquaporin-2

Adrenal Cortex

Adrenal cortex secretes 3 major steroids

1. Mineralocorticoids — from zona Glomerulosa
 2. Glucocorticoids — from zona Fasciculata
 3. Sex steroids (androgens) — from zona Reticulata
- [mnemonic GFR]

→ DHEAs are androgens synthesized from ZR of adrenal gland.

→ In renal glycosuria renal threshold for glucose is low

→ Urea have no T_m (Tubular maximum) value.

→ Maximum urine acidity 0.03, normal urinary pH = 5.85, specific gravity 1.015-1.025

→ Daily loss of N_2 in urine 20-50 gm.

Glucocorticoids

- Cortisol (hydrocortisone) is the major glucocorticoid in humans
- Receptors are present predominantly in the cytoplasm. Inactive receptor binds with heat shock protein 90.

Mineralocorticoids

- Aldosterone is the main mineralocorticoid
- Mineralocorticoid **receptors** are expressed principally in the *kidney* (distal cortical tubules and collecting ducts of nephron) and also in colon, salivary glands, sweat glands and *hippocampus* [but NOT in the liver].
- Aldosterone regulates Na^+ & K^+ homeostasis. It acts on principal cells of distal cortical tubules and collecting duct
- Aldosterone enhances reabsorption of Na^+ and also \uparrow es urinary excretion of K^+ and H^+ .
- Aldosterone causes diastolic hypertension without edema.

Effects of Thyroid Hormone

- \uparrow ed HR to meet the \uparrow ed oxygen needs.
- T_3 directly boosts energy metabolism in mitochondria.
- Stimulates brown adipose tissue, a mitochondria-rich tissue, to boost **heat production** in mammals without muscle activity.
- Triggers rapid protein synthesis.
- Estrogen partially blocks the efficiency of thyroid hm, so women compensate by producing more thyroid hm than men

REPRODUCTIVE SYSTEM

SPERMATOGENESIS

- Spermatogonia begin to \uparrow se in number at puberty (13-16 years of age in male)
- After several mitotic divisions, spermatogonia grow & undergo changes to form 1^0 spermatocytes (largest germ cells in the tubules)
- Each 1^0 spermatocyte undergoes a reduction division called the first meiotic division to form 2 haploid 2^0 spermatocytes (half the size of primary). 2^0 spermatocytes undergo a second meiotic division to form 4 haploid spermatids (half the size of secondary spermatocytes)
- The spermatids gradually form 4 mature sperm or spermatozoa via spermiogenesis

Primordial germ cells



Spermatogonium (Primitive germ cell)



Primary spermatocyte



1st meiotic division



2^0 spermatocyte



2nd meiotic division



$22 + X$ $22 + X$ $22 + Y$ $22 + Y$

Spermatids



Androgens



Mature spermatozoa

→ Until 6th wk of development primitive gonads (int. genitalia) are apparent as genital ridge in both sexes. Male and female morphological characteristics are established after 7th week.

→ A single spermatogonia gives rise to 512 spermatids.

→ Secondary spermatocyte is haploid & n.

→ Spermatogenesis requires a temperature considerably lower viz $32^\circ C$ ($-5^\circ C$ or) than the body temperature. Testes are kept cool by airing around scrotum & countercurrent system.

→ Spermiogenesis is --- conversion of spermatids into mature spermatozoa.

→ Spermatogenesis & meiosis occurs in — seminiferous tubules.

OÖGENESIS

Yolk sac → (Primordial germ cells)



Oogonium (Primitive germ cell)



Primary oocyte (Present inside graffian follicle) +nt at birth

↓ *Arrested in prophase of 1st meiotic division upto puberty*

2⁰ oocyte 1st polar body

↓
Ovulation

(Metaphase of 2nd meiotic division completes only when sperm penetrates oocyte)



Not fertilized

Fertilization



Degeneration

2nd polar body

Female pronucleus

- Primordial follicles develop from yolk sac.
- Number of follicles in female newborn - 2 million
- The ovaries have roughly 2 million primordial follicles at birth, each containing a primary oocyte. By the time of puberty, the number has dropped to about 400,000.
- Zona pellucida is maintained upto secondary oocyte stage, when implantation is imminent (about 5 to 6 days)
- First polar body is extruded approx. 24-36 hours prior to ovulation & accompanied by completion of meiosis I

Sperms

- Antifertilizin is secreted by sperm and fertilizin by ovum (Mnemonic—FOFA)
- Acrosomal reaction -
On reaching ovum, acrosome of sperm releases lysosomal enzymes.
 - Hyaluronidase : helps in penetration of corona radiata.
 - Trypsin like substances and acrosin : helps in dissolving zona pellucida (zona reaction).
- Transformation of an immature germ cell or spermatogonium into a mature sperm takes about 64 days. Length of mature human spermatozoa is --- 50-60 micron. Whip-like tail (flagellum) of the sperm is studded with ion channels formed by proteins called CatSper. The opening of CatSper channels is responsible for the influx of calcium

- In sperm – Acrosomal cap develops from Golgi apparatus

- Tail (Flagellum) develops from one of the two centrioles
- Middle piece of spermatozoa develops from Mitochondria

- After formation sperm are stored, become mature & motile in--- distal epididymis (Become fully motile only after ejaculation in FGT).
- Spermatozoa on reaching the fallopian tube under go some changes, collective k/as sperm capacitation.
- Fructose, Lactate, and Acetyl carnitine are imp. for sperm motility.
- Human ovum survive ~24 hrs after ovulation if it is not fertilized.
- In female genital tract sperms survive for 48 hours (range 1-5 days).
- Sperm moves at rate of 3 mm/min in FGT. (fructose is the principle fuel for sperm motility).

Male Reproductive Organs

- Testes --- Testes are placed in scrotum at a temperature which is considerably lower than the core body temperature. This temperature ~ 32° C provides favorable milieu for spermatogenesis. This low temperature is maintained by circulating air current and counter current heat exchanger system b/w spermatogenic arteries and veins.
- Seminiferous tubules
 - The spermatozoa (sperms) are synthesized in seminiferous tubules. The pathway of sperms from within the testes to the epididymis is
Seminiferous tubule → straight tubules → Rete testes → efferent tubules → epididymis
 - Secrete testosterone/ androgens (through Leyding cells/ interstitial cells of Leyding)
 - Maturation and nourishment of sperms (through Sertoli cells)
- Epididymis --- Stores sperms and provide motility
- Ductus deferans --- Transports sperms.
- Sperm Characteristics.
 1. Length: 65 mm
 2. Number: 100 million per ml of semen
 3. Motile at emission: more than 80%
 4. Rate of movement in the genital tract: 5 mm per minute.
 5. Survival in the genital tract: 3 to 4 days.

Semen

Components of semen are

1. Spermatozoa from seminiferous tubules,
2. Seminal fluid is thick and alkaline which contains coagulant from **seminal vesicles**, *Fructose*, choline, vitamin C, prostaglandins, hyluronidase)
3. Prostatic fluid is thin & milky. It contains acid phosphatase, cholesterol, zinc, spermine, citric acid, phospholipids etc.)
4. Some other enzymes to liquefy semen from prostate gland.

Semen is slightly alkaline fluid with pH 7.35- 7.50, rich in phosphates and HCO_3^- , sperm count ~ 100 million/ml (80% motile).

Sequence of Pubertal Events

Sequence	Male	Female	~ Age (M/F)
1.	Adrenarche	Adrenarche	7
2.	Gonadarche	Thelarche	8 (M)11(F)
3.	Pubarche	Pubarche	12
4.	Spermarche	Menarche	12.5

- Gonadarche (*Testicular enlargement*) is the first visible sign of puberty in boys.
- **Thelarche** (*appearance of breast buds*) is the first sign of puberty in females.
- In male Pubic hair → Axillary hair → Beard
- Adrenarche is the first event in both males and females.
- The development of secondary sexual characteristics is initiated by **adrenarche** (which occurs b/w 6-8 yrs) when adrenal glands start producing androgens from zona reticularis zone. Puberty is preceded by adrenarche, marking an increase of adrenal androgen production between ages 6-10. Adrenarche is sometimes accompanied by the early appearance of axillary and pubic hair. The first androgenic hair resulting from adrenarche can be also transient and disappear before the onset of true puberty.
- Growth spurt is overlapping, may start even before thelarche/gonadarche.
- Peak height velocity (**maximum growth velocity**) usually occurs at the age of 14-15 yrs, which may be ± 1 yr to menarche/spermarche.

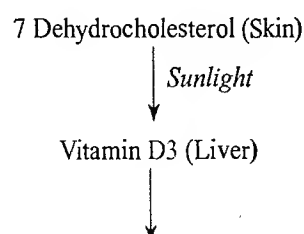
ENDOCRINOLOGY

Calcium Homeostasis

Features	PTH	Vitamin D	Calcitonin
Secreted by	Parathyroid glands	Skin (vit D3), Liver (CC)	Parafollicular (C-cells) of thyroid
Stimulus for secretion	$\downarrow \text{Ca}^{++}$	$\downarrow \text{Ca}^{++}$ $\downarrow \text{PTH, P}$	$\uparrow \text{Ca}^{++}$
Receptors present on	Osteoblasts	Osteoblasts	Osteoclasts
Bone resorp ⁿ	\uparrow	\uparrow	\downarrow (osteoclast inhibition)
Kidney: PO_4^- reabsorp ⁿ	\downarrow (phosphaturic)	\uparrow	
Proximal tubular Ca^{++} reabsorp ⁿ	\uparrow	\uparrow	\downarrow (calciuric)
Gut : Ca^{++} reabsorption	\uparrow	\uparrow	
Net effect			
Serum calcium	\uparrow	\uparrow	\downarrow (hypocalcemic hm)
Serum phosphate	\downarrow	\uparrow	\uparrow

- Calcitonin is a hypocalcemic hormone. It inhibits the osteoclasts → thus inhibits bone resorption & also \uparrow calcium excretion (calciuric) → hypocalcemia. It is useful in Paget's d/s, post menopausal osteoporosis, hypocalcemic states (hyperparathyroidism), hypervitaminosis D, osteolytic metastasis.
- Parathormone activates Vit D → \uparrow es Ca^{++} absorption from proximal small intestine thus it indirectly \uparrow Ca^{++} absorpⁿ. PTH also promotes reabsorpⁿ of filtered calcium from proximal tubules of kidney
- Calcium absorption is facilitated by proteins & inhibited by phosphates, phytates, oxalates.
- Skin is involved in calcium homeostasis as a source of vitamin D3 (Cholecalciferol) with the help of UV rays of sunlight.

The metabolic pathway of Vitamin D



25 OH vitamin D (Kidney)



1,25 Di OH vitamin D3

Pituitary hormones

Anterior pituitary hm (adenohypophysis)		Posterior pituitary (neurohypophysis) hm
Acidophil cells	Basophil cells	
GH (from somatotrope)	ACTH TSH	Oxytocin ADH (AVP or vassopressin)
Prolactin (from lactotrope)	FSH, LH (from gonadotropes cells)	

Applied aspect

- ↑ GH and ↓ somatomedin levels are seen in Kwashiorkor
- Congenital abnormality of GH receptors — Laron dwarfism
- ↑↑ GH during adolescence (before epiphyseal fusion) results in — Gigantism (giantism)
- ↑↑ GH after epiphyseal fusion results in — Acromegaly (M/c cause of acromegaly is acidophil tumour of anterior pituitary)

Gonadal Hormones : LH and FSH

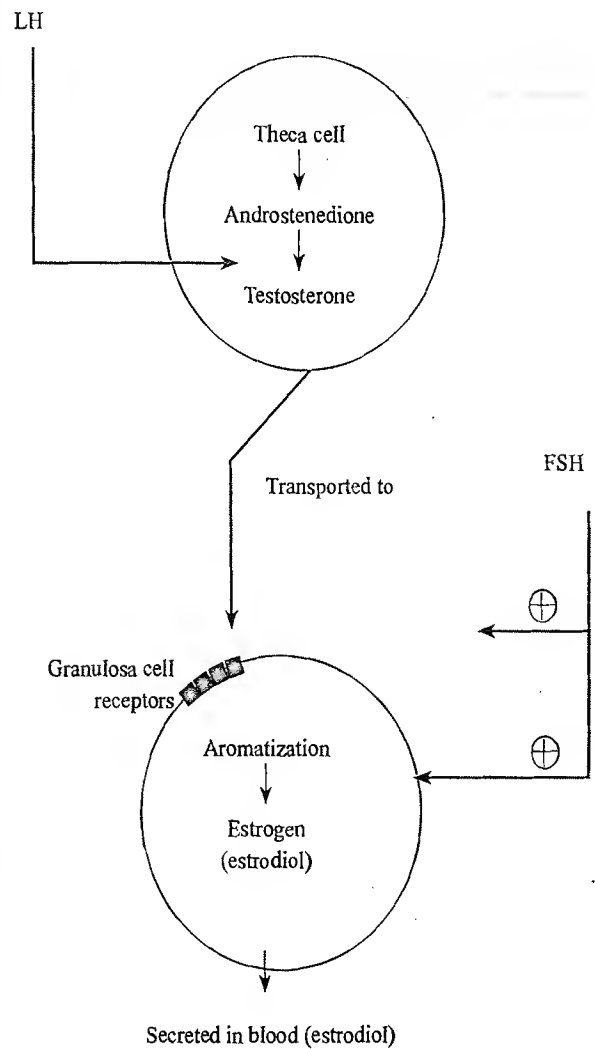
Role / Function	LH	FSH
1. Ovarian follicle growth	Final maturation	Early growth
2. Aromatase activity	-	+ nt
3. Role in formation of CL, progesterone secretion	+	-
2. Aromatase activity	-	+ nt
2. Receptors present on	Granulosa cells, theca interna in females Leyding cells in males	Granulosa cells in females Sertoli cells in males

- LH acts only on FSH primed granulosa cells. FSH ↑ no. of receptors for LH to act upon. Aromatase catalyzes conversion of androstenedione to estrone and testosterone to estradiol.

- Ovarian reserve is indicated by FSH.

Indicators of poor ovarian reserve are — Advancing age, ↑ FSH > ↓ Inhibin.

- Inhibin & follistatin suppress FSH → Delay puberty
- Activin A activates puberty → Early puberty
- High prolactin levels are a/w high FSH.

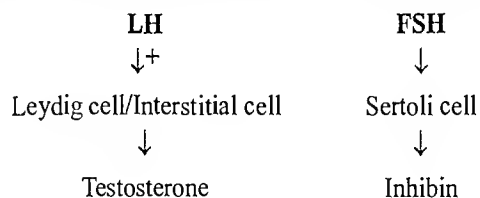


Sertoli cells

- Form blood testes barrier
- Secrete ABP, inhibin & MIS & contain aromatase enzyme (can convert androgens to estrogen)
- They are phagocytic and provide physical support and nutrition to germ cells.
- They have receptors for the FSH and testosterone. They stimulate first half of spermatogenesis.
- They aid in spermiogenesis by nursing developing sperm cells.

Testosterone

- Inhibit LH & FSH secretion (in high concentration)



- Testosterone in embryo is synthesized from hCG.

Inhibin

- Produced by **Sertoli cells** in males (mainly). In females it is produced by granulosa cells of graafian follicles of ovary during follicular phase.
- Strong inhibitor of FSH secretion, that's why it is called inhibin
- Non steroidal water soluble protein; secretion increased in PCOD

MIS

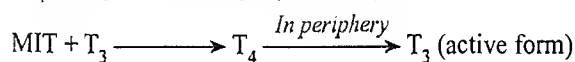
- Also k/as Mullerian inhibiting substance or Mullerian regression factor.
- Secreted by Sertoli cells in males in both fetal life & also in postnatal life and by granulosa cells in small follicles of ovary in females postnatally
- Probably involved in germs cell maturation (in male and female both). In *testicular descent* (in male).

Relaxin

- Secreted in females by CL of ovary and placenta
- Relaxes pubic symphysis during labour (*augments labour*)
- *Structural similarity with insulin and IGF*

T3 Vs. T4

- T_3 is more active, more potent and has maximum affinity for albumin
- T_4 is inactive and more tightly bound to plasma protein (T_4 is major circulating thyroid Hm)



SOMATOMEDINS

- Polypeptide growth factors secreted by liver and other tissues.

- Somatomedin -C is also k/as IGF-I, mainly involved in skeletal and cartilage growth. It mediates chondroitin sulfate deposition.
- MSA or IGF-II is mainly involved in growth during fetal development.

HORMONES IN STRESS

- Secretion of stress hormone increased --- Epinephrine, Nor Epinephrine, cortisol, glucagon
- ↓ secretion of anabolic hormones --- insulin, testosterone
- Stress induced hypoglycemia is mediated by --- Epinephrine, cortisol, glucagon (by stimulation of gluconeogenesis)
- Increased lipolysis.
- Mild hemorrhage leads to : ↑ ACTH, ↑ aldosterone, ↑ sympathetic activity → ↑ TPR, ↑ venoconstriction .

SOME POINTS OF SPECIAL MENTION

- *Arteries of body where $P_{CO_2} > P_{O_2}$* :
 - Pulmonary a.
 - Gastric a.
- *Deoxygenated blood flows through*
 - Pulmonary a.
 - Systemic veins (e.g. Renal vein)
 - Umbilical a.
- Chronic cold exposure leads to activation of sympathoadrenomedullary system.
- Rouleaux formation ↑ *es when plasma fibrinogen and gammaglobulin ↑ (viscosity ↑) as in most acute and chronic infections, inflammations, RA, TB etc. ESR also ↑ es.*
ESR ↓ in CCF, PV & sickle cell disease.
- Most potent vasoconstrictor : Endothelin-1 > Angiotensin-II > Renin
- Olfactory sensory neurons are unique among sensory system in that they are regularly replaced and regenerate after injury (bipolar cells have capability to regenerate). Receptors of olfaction and pain itself are dendrite of a nerve.
 Olfaction and gustation appear unique among sensory system in that at least some fibres bypass the thalamus.
- Muscle can tolerate hypoxia for 1 hour and nerves for ½ hour.
- Sense of olfaction goes directly into the brain (olfactory cortex of the frontal lobe) without going through the thalamus. Its the only major sense that does not go through the thalamus.

• Type of cells in lungs

- Type I pneumocytes : Phagocytic function
- Type-II pneumocytes : Secrete surfactant

Comparative functions/Histo of liver, spleen, kidney, BM

Structure	Histo	Functions/ Synthesis of
Liver	Kupffer cells Space of Ito Cords of Billroth	Amyloid associated protein, Albumin Clotting factors 2,7,9,10, 1, 5 Transferrin, Angiotensinogen
Spleen		Heme breakdown Complement
Kidney	Malpighian corpuscles Ansa nephroni	1, 25 DHCC Renin Erythropoietin
Bone marrow	Pluripotent stem cells	RBCs synthesis in adult B lymphocytes

• Type of cells in synovial fluid

- Type A cells : Phagocytose joint debris
- Type-B cells : Secrete synovial fluid

- Ambient pressure ↑es by 1 atm.at every 10 meter (=33 feet) depth in sea water

So normal atmospheric pressure which is 1 atm will be 2 atm at 10 m (33 feet depth) sea level 3 atm at 20 m (66 feet) & 4 atm at 30 m

- Blood nerve barrier is reinforced by cells of perineurium. It separate peripheral nerves from circulating blood.

SOME IMP. NEGATIVE POINTS

- Spirometry do NOT measure --- FRC, TLC, RV.
- Appetite is NOT increased by ---MSH
- NOT seen in sympathetic stimulation --- Increased refractory period.
- Collagen --- is NOT present freely inside the cytoplasm
- Iron absorption is NOT decreased by --- Vit. C
- NOT true in exercise--- Shifting of oxygen dissociation curve to the left.

- Hematocrit --- value NOT changes with age.
- ABO antigens are NOT found in --- CSF
- Calcitonin --- is NOT required for G.I. absorption of calcium.
- Factor which is NOT responsible for venous return during standing --- Arterial pulsation
- NOT an effect of insulin --- Gluconeogenesis
- NOT seen in Emphysema --- ↑ FEV₁ & ↓RV
- NOT required for G.I. absorption of calcium --- Calcitonin.
- NO role in mucin secretion --- Paneth cells
- CCK-PZ (Cholecystokinin) does NOT cause --- Increase gastric secretion.
- NOT an effect of insulin --- Gluconeogenesis
- Glomerular Filtration barrier is NOT formed by --- Mesangial cells
- NOT involved in calcium homeostasis --- lungs
- Hypoxemia is NOT dependent on --- Hb
- NOT seen in intrinsic pathway --- Factor XIII
- NOT a stimulant of growth of fetal microvessels in eye --- FGF
- NOT a function of angiotensin --- Vasodilatation
- NOT absorbed from PCT --- H⁺
- Does NOT have sympathetic supply --- Brain.
- 2,3 DPG is NOT influenced by - CO₂ or temperature.
- Physiological/resting ventilation is NOT affected by --- J-receptors
- Mineralocorticoid receptors are NOT found in --- Liver

NOTES

AMINO ACIDS (AA)

Important amino acids

Proteins are effective buffers of body and ICF. buffering capacity is dependent upon presence of a/a having ionizable side chain with pk values near physiological pH. Maximum buffering capacity occurs at $pK_a \pm 1$ pH unit. Strong acids have low pK_a value and weak acids have high pK_a value.

Amino acid	Type	pK	Remark
<i>Essential</i>			
Arginine	Basic, semi-essential	12.48	Most basic, precursor of NO
Histidine	Basic, semi-essential	6.00	Active at neutral pH
Lysine	Basic	10.53	
Iso-leucine	Branched chain aliphatic		
Leucine	Branched chain aliphatic		Most non-polar & only ketogenic a/a
Valine	Branched chain aliphatic		
Threonine	Aliphatic hydroxyl		
Phenyl alanine	Aromatic		
Tryptophan	Aromatic		Precursor of niacin
Methionine	Sulfur containing		Precursor of homocysteine
<i>Non-Essential</i>			
Cysteine	Sulfur containing		Responsible for reducing action of glutathione
Alanine	Aliphatic		
Asparagine	Unchanged polar		
Aspartate	Acidic	3.86	
Glutamate	Acidic	4.25	
Glutamine	Unchanged polar		Most abundant a/a in blood, Optically inactive
Glycine	Aliphatic		Simplest a/a, flexible, present in heme, Optically inactive
Proline	Cyclic aliphatic		Protein reversal, Not present in α -helix,
Serine			
Tyrosine	Aromatic		Forms T_3 , T_4 , E, NE, melanin

Essential /Indispensable a/a

- These are 9 in number and include **methionine, arginine, threonine, tryptophan, valine, isoleucine, leucine, phenylalanine, lysine (MATT VIL F(Ph)Ly)** [Remember T is not tyrosine & A is not alanine]
- Arginine** is nutritionally semiessential, becomes essential in growing children. Same is true to some extent for histidine
- Tyrosine becomes essential a/a in phenylketonuria.
- In general essential a/a are glucogenic while non-essential a/a are ketogenic.

Imino acids

Proline, OH-proline, **selenocysteine** (the 21st amino acid). **Selenocysteine** is involved in post translational modification.

Amino acids with non- polar side chain

- Leucine (most non-polar) > valine, proline, phenylalanine, methionine, alanine
- Leucine & valine are a/a with uncharged i.e. non-polar and branched side chains

Basic amino acids

Arginine > lysine > histidine

Sulphur containing amino acids

- Cysteine, cystine, and methionine
- Urinary sulphates are mainly derived from these sulphur containing a/a.

Aromatic amino acids

- Amino acids with aromatic ring : Phenylalanine, tyrosine, histidine, tryptophan.
- All aromatic amino acids are derived from alanine.
- Aromatic a/a exhibit property of *photochromicity*. Emits UV at wavelength 250-290 nm esp at 280 nm. Photochromicity is max^m with tryptophan. Tryptophan > tyrosine > phenylalanine
- Melatonin is synthesized from tryptophan & melanin from tyrosine**
Tryptophan → Serotonin → Melatonin
Phenylalanine → Tyrosine → E, NE, T3, T4 & Melanin

- Niacin is synthesized from tryptophan.
- Xanthurenic acid is a bi-product of tryptophan metabolism and is found in blood & urine with aging.

Histidine

- Only **Histidine** has ionizable imidazole gp that has a pK value close to neutrality (pK = 6.0). The imidazole group can pick up or release protons readily at pH 7. Frequently involved at the active site of enzymes
- Greatest buffering capacity. Maintains optimal blood pH. Most stable at physiological pH.
- Decarboxylation provides histamine
- Level ↓ es in normal pregnancy d/to histidinuria.

- Amino acids which are glucogenic & ketogenic both - lysine, Phenylalanine, Tyrosine, Tryptophan, Iso-leucine [Mnemonic : LyPHTTI]
- Only ketogenic (fat forming) amino acid is :- l-leucine
- Most non-polar a/a → L-leucine
- Amino acids producing hypoglycemia — leucine (ketogenic) and arginine (↑ insulin release)
- Aspartate & Glutamate are monoamino di-carboxylic acid
- Glutamate is precursor of arginine, proline, glutamine (Mnemonic : GAP)
- Hb can act as buffer at physiological pH because of high content of histidine
- All a/a except glycine exists in D & L isomer. Glycine has no asymmetric carbon atom, so it does not show stereo isomerism & optical isomerism.
- Allo-threonine is amino acid which can exist as a diastereomer.
- There are no t-RNA for — OH-proline, γ carboxy glutamate, OH-lysine
- Amino acid a/w atherosclerosis & ↑ risk of CAD — homocysteine (hyperhomocysteinemia)
- Zwitter ion are molecules with no net charge i.e. have positive ions = negative ions
- Isoelectric point is the pH at which an amino acid bears no net charge
- Glycine is the fundamental building unit (forms building blocks).

Amino acids required for Sp. products

- Creatine : Glycine + Arginine + Methionine (GAM)
- Purine : Glycine + Aspartate + Glutamine + serine (GAGS)
- Pyrimidines : Aspartate + glutamine
- Glutathione : Glycine + Cysteine + Glutamate (GCG)
- Histone : Protein rich in arginine + histidine, basic protein (Hi Argi)
- Carnosine : β-alanine + histidine, dipeptide of skeletal & heart muscles (Hi Allen)
- Hemoglobin : A/a for Hb synthesis are Histidine + Lysine + Arginine (HLA or Hi ArgiLy)

- Keratin : Formed by Histidine : arginine : lysine (1 : 12 : 4) (HLA or Hi ArgiLy)
- Choline : Methionine, glycine, serine, B₆
- Carnitine : Formed from lysine + methionine

- Flexibility of protein is d/to glycine as it is simplest a/a.
- Proline reduces flexibility of proteins. Used in synthesis of fibrous part of collagen.
- Elasticity of cornified skin is d/to keratocysteine content of cells.
- In carboxylation of clotting factors by vitamin K, a/a glutamate is carboxylated.
- Dentin of enamel is the hardest substance of the body.

Glutathione

- Tripeptide containing G-C-G
- It is an important intracellular reductant /reducing agent.
- Role in xenobiotic (conjugation reactions)
- Converts methHb to Hb and helps to maintain essential SH-group of enzymes.

Chaperones

- Chaperones are accessory proteins or "heat shock proteins" (hsp).
- They prevent faulty folding and aggregation of other proteins. They act as a quality control or editing mechanism for detecting defective proteins.
- They bind short sequences of hydrophobic end in newly synthesized polypeptide chain, shielding them from solvent (hsp-70) & provide an environment for elements of 2° structure to emerge & coalesce into molten globules.
- Proteins that assist folding include — protein disulphide isomerase, proline cis-trans isomerase & chaperons
- Abnormal folding of proteins (β-amyloid), unassisted by chaperones, leads to Alzheimer's disease.
- Prion diseases (e.g. CJD) which are fatal neurodegenerative diseases result from altered protein conformation. Infectious proteins with correct primary structure & wrong tertiary structure.

Glycosaaminoglycans (GAGs)

- The major GAGs are --- hyaluronic acid, chondroitin sulfates, keratan sulfates I, and II heparin, heparan sulfate, and dermatan sulfate
- GAGs are made up of repeated disaccharide units containing a uronic acid + hexosamine
- Hexosamine may be either galactosamine or glucosamine

- Uronic acid is either glucuronic acid or iduronic acid
- GAGs are degraded by lysosomal hydrolases. Genetic deficiency of this degrading enzyme results in MPS/Hurler's syndrome.

PROTEINS

Imp. proteins/ Classification

- *Structural (fibrous) proteins*
Fibrous proteins of skin, cartilage, hairs, nails (e.g. collagen proteoglycans). They contain α -keratin
- *Globular proteins*
Storage/transport proteins. E.g. Hb, Mb, albumin and globulin are simple globular proteins

Structure of proteins

Proteins are synthesized as a primary sequence and then fold into secondary \rightarrow tertiary \rightarrow and quaternary structures. Amino acids are the building blocks (units) of proteins. The amino acids of a protein are connected to each other by peptide bonds

Primary structure

The linear sequence of amino acids constitutes a protein's primary structure. Stabilized by covalent peptide bonds (strongest bond). All properties of a protein are derived from the primary structure, the linear sequence.

Secondary structure

Arise from **non-covalent** interactions b/w amino acids. Stabilized by multiple H_2 - bonds, sulphide bond.

1. α - Helix
Intra-chain hydrogen bonding. eg. Hair, nails and skin are rich in keratin & thus in α - helix. (proline is absent in α - helix)
2. β - Pleated sheet structure
Inter chain hydrogen bonding. β -keratin in silk fibres proline is present (causes kinks)
3. Triple Helix
Found in collagen (glycine is present at every 3rd position).
Inter chain hydrogen-bonding

Tertiary

The term "tertiary structure" refers to the entire 3-D confirmation of a polypeptide. Major interactions are hydrophobic. Other

weak bonds are ionic/salt/electrostatic, Vanderwal, H_2 bonds. Vibratory property is seen using *X-ray diffraction*.

Quaternary

Peptide bonds do not take part in formation of this bond. Examples of quaternary structures are : hemoglobin, immune complexes/ antigen-antibody complexes, DNA polymerases, ion channels, nucleosomes, microtubules etc.

- \rightarrow Higher order of proteins (3^0 and 4^0) are stabilized primarily & exclusively by non-covalent interactions
- \rightarrow Di-sulphide bonds are strong high energy covalent bond, present in insulin, cystine, immunoglobulin etc.
- \rightarrow Strength of diff. bonds — Covalent bond (strongest) > disulphide > electrostatic (salt linkage or ionic bonds) > hydrogen bond > vanderwall forces (weakest)
- \rightarrow A carboxyl group makes a carbon based compound the least polar, while an amino acid group makes it a stronger acid.
- \rightarrow Level of protein structure in immune complex — Tertiary.

Analysis of protein structure

1. Primary structure - Amino acid composition is determined by:
 - (a) Hot-acid hydrolysis.
 - (b) Ion-exchange chromatography identify amino acids sequence by Edman reaction.
2. Secondary & tertiary structure
 - X-ray crystallography (X-ray diffraction method.)
 - Studies of protein in solution (UV-spectroscopy.)

- \rightarrow Keratin of nail is stronger & harder than that of skin because there are less S-S bonds in skin keratin. If the number of disulfide bond increases, stability of the flexibility decreases.
- \rightarrow 3-D structure of proteins is determined by X-ray crystallography or by NMR spectroscopy.
NMR spectroscopy analyzes proteins (≤ 30 kDa) in aqueous solution
- \rightarrow Renal and Gall stones are analyzed by X-ray diffraction, polarizing microscopy and infrared spectroscopy.
- \rightarrow Tertiary structure of cytochrome C is highly conservative, explains for functional plausibility.
- \rightarrow Proteins whose charges are same, can be separated by gel diffusion chromatography
- \rightarrow Most widely used method for determining the purity of proteins is SDS-PAGE
- \rightarrow M/c method of analyzing plasma proteins is by electrophoresis

Separation and purification of proteins

There are various techniques used to separate proteins from one another. These techniques are based on a peculiar property like solubility, size of protein molecules, and charge etc.

Solubility	1. Salting in/out
	2. NH_4SO_4 precipitation
Molecular size, mass (or weight)	1. Dialysis/ultrafiltration
	2. Gel filtration chromatography or size exclusion molecular exclusion/ sieving/ <i>Sephadex</i> .
Molecular charge	3. Ultracentrifugation.
	SDS-PAGE
	4. Chromatofocussing, Denaturing gel
	1. HPLC
Molecular charge	2. Electrophoresis
	3. Ion exchange chromatography. [<i>DEAE cellulose/ CM cellulose</i>]
	4. Isoelectric focussing

- Iso-electric focussing (IEF) separate proteins on the basis of isoelectric pH (pI).
- Ion exchange chromatography is used for free amino acids & Gas liquid chromatography for fatty acid.
- Methods of separation of proteins by binding specificities ---Affinity(absorption) chromatography, precipitation by antibodies.
- Protein purity is assessed by PAGE. The most widely used method for determining the purity of protein is SDS-PAGE (PolyAcrylamide Gel-Electrophoresis).
- In Western Blot technique protein separation is done by --- SDS-PAGE.

Chromatography Methods

Chromatography is separation of molecules depending on the relative affinity of different proteins for a given stationary phase and for mobile phase.

Column chromatography

Based on their charge, hydrophobicity, and ligand binding properties.

Chromatography Type	Protein separation based on	Remark/use
• Ion exchange	Charge	Cation (Carboxymethyl sepharose) Anion (DEA sepharose)
• Reverse phase	Hydrophobicity	
• Affinity	Ligand binding	Purification of enzymes

- Edman technique was used for determining the sequences of peptides and proteins.
- Molecule with large non-polar R group move faster on paper chromatography e.g. Leucine, isoleucine, valine, PA, tryptophan, tyrosine, methionine)
- Mass spectrometry detects covalent modifications. It has replaced the Edman technique as principal method for determining the sequences of peptides and proteins.

Collagen

- All collagens have a **triple helix** structure.
- A striking characteristic of collagen is the occurrence of **glycine residue at every third position** of the triple helical portion of α -chain (as glycine is the simplest a/a, it can accommodate in limited space).
- **Proline and hydroxy proline** provide rigidity.
- *Important types and associated d/s.*

Type	Most abundant in	D/s a/w defect in collagen	Mutation in
Type I	Most connective tissues and bone	Osteogenesis imperfecta	COL1A1
Type II	Cartilage and vitreous humour	Chondrodysplasias	
Type III	Skin, lung, vessels	Ehler-Dalos Syndrome, most severe form	
Type IV	Basement membrane	Alport syndrome	
Type VII	Basement membrane	Dystrophic Epidermolysis bullosa	COL7A1

- Collagen synthesis requires following enzymes
 - Propyl hydroxylases (which require cofactors Vit. C & α -KG) are involved in **post translational modifications**
 - Stabilized by formation of covalent cross-linkage through the action of enzyme lysyl oxidase, a copper dependent enzyme which is involved in **oxidative deamination** of lysine/ OH-lysine.
- Diseases a/w impaired collagen synthesis are Scurvy, osteogenesis imperfecta, EDS, Menkes d/s.
 - Vitamin C is required for post-translational modification of procollagen polypeptides in collagen synthesis
 - Vitamin K is the coenzyme required for post translational modification (carboxylation) of glutamate residue in clotting factor synthesis to form the unusual amino acid γ -carboxyglutamate (Gla)
 - D/s of collagen maturation include Ehlers-Danlos syndrome & scurvy.
 - Laminin is the major protein present in GBM of kidney
 - Filaggrin is a hyaline rich protein which acts as interfilamentous glue to aggregate and align keratin filaments

Elastin

- Confers extensibility and elastic recoil on tissues.
- It lacks triple helix structure, Gly-X-Y sequences, and sugars but **contains desmosine and isodesmosine** cross links which are not found in collagen

METABOLISM

- *SDA (Specific Dynamic Action)* is overheat/extra heat produced by food stuff in vivo (from expected in vitro).
- *Lipotropic factors (lipotropins)* are Inositol, Betaine, Methionine, Casein, lecithin, Androgens, GH, Choline (Either they contain or synthesize choline). **Choline** is the most important lipotropic factor and it prevents fatty liver.
- *Anti-lipotropic factors* are nicotinamide, guanidoacetic acid.

Metabolic fuels & energy production

- CBH (Glucose, Glycogen) --- 4 K cal /gm
- Amino acids on average, proteins --- 4 K cal /gm
- Ketone bodies (hydroxybutyrate/ acetoacetate) --- 4 K cal /gm
- Alcohol --- 7 K cal /gm
- Fatty acid --- 9 K cal /gm

→ Calorie provided under basal conditions— 60% by fats, 35% by carbohydrate and 5% by ketones. Proteins are meant for growth and immunity.

Substrates for energy in metabolic states

Organ	Well Fed state	Fasting	Starvation
Muscle	Glu	FA	FA
Liver	Glu	FA	AA
Brain	Glu	Glu	KB
Heart	FA	FA	KB

- Skeletal m/s maintain large stores of glycogen which provide a source of glucose for energy during exertion.
- In resting muscles preferred fuel is fatty acids.
- Fatty acids are major fuel source for heart, renal cortex, adipose tissues.
- Retina completely depends upon glucose as a fuel source.

Metabolism in Starvation

- Occurs after 2 or 3 days without food.
- Initially ↑ed gluconeogenesis from a.a then ↓es
- Order of mobilization

1st stage	2nd stage	3rd stage
Liver glycogen	→ fats (FA & ketones)	→ tissue protein
- Hypoglycemia depress insulin secretion & glucagon activity ↑es it. (↓in insulin :glucagon ratio)
- In starvation, **alanine and glutamine** are the most important source for gluconeogenesis.

- KB formed in starvation are --- acetoacetate and β-hydroxybutyrate
- **Ketoacidosis occurs without hyperglycemia & glycosuria** (less severe than DKA).
- During prolonged starvation, the rate of gluconeogenesis depends on ↑es alanine in the liver.

Metabolism in Well Fed /absorptive phase

- Insulin suppresses G-6-phosphatase activity → G-6-P to enter glycogenesis pool to form glycogen
- In well fed state only heart utilizes fatty acids, while m/s, liver & brain utilize glucose as a substrate for energy production.
- Malonyl CoA, the intermediate in FA synthesis is a potent inhibitor of CPT-1

Ketosis

- Ketosis occurs in liver.
- Ketosis is metabolic adaptation to starvation. Ketone bodies are synthesized in starvation NOT in well fed state
- KB are derived from acetyl Co A & they serve as fuel for extrahepatic tissues in starvation & uncontrolled DM
- Ketosis of starvation differs from ketosis of DM --- Ketosis of diabetes (DKA) is more severe, a/w hyperglycemia & glycosuria.
- I/V administration of glucose in relatively small amount abolishes the ketosis, that's why the carbohydrate is said to be anti-ketogenic.

- Acetoacetate is most important KB as it can form acetone & β-OH butyric acid both.
- β-OH butyrate is predominant KB of blood / urine but it is not a true ketone.
- Acetoacetyl CoA is starting material and HMG CoA synthetase is rate limiting step for K.B. synthesis.
- Acute liver failure with ↑ketones is seen in Reye's syndrome.

Metabolic adaptations in Alcoholic

- Basis of fatty liver is ↑ NADH/ NAD⁺ redox ratio which leads to → accumulation of fats (mainly in form of triglycerides) in liver.
- Fatty liver is caused by a combination of impaired FA oxidation & ↑ lipogenesis.

NADPH

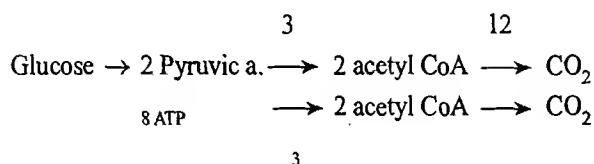
- Produced by → Pentose phosphate pathway.
- Required for → Fatty acid synthesis, steroid synthesis, Glutathione reductase
- NADP is reduced in anaerobic pathway to lactate.

Metabolism of Glucose

	Glycolysis	TCA/ Citric acid cycle	HMP
Also k/as	EMP pathway	Kreb's, TCA cycle	PPP pathway
Occurs in	Cytosol	Mitochondria	Cytosol
Conversion	Metabolism of glucose/ glycogen (6C) → pyruvate and lactate (3C unit)	Oxidation of acetyl coA with production of ATP by reducing co-enzyme	
Begins with	Glucose/ glycogen	Pyruvic acid	G-6-P oxidation
End Product	Pyruvate (under aerobic condit ⁿ) Lactate (under anaerobic condit ⁿ)	CO ₂ + H ₂ O —	G-5-P 6CO ₂ + 12 NADPH ₂
Energy production	10 ATP total produced. But net gain	12 ATP	NOT meant for energy
Per glucose molecule	8 (10-2) under aerobic condit ⁿ		Produces NADPH and
net gain	2 (4-2) under anaerobic condit ⁿ		Ribose

GLYCOLYSIS

- In glycolysis there occurs incomplete breakdown of glucose as pyruvate further enters mitochondria to be completely degraded into CO₂ + H₂O. 1 molecule of glucose after complete oxidation produces total 38 ATP (glycolysis + 2Kreb's) under aerobic conditions and only 2 ATP under anaerobic conditions.



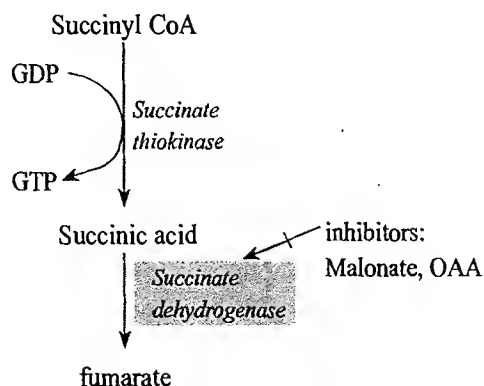
- There are only 2 steps in glycolysis where substrate level phosphorylation occur with production of 1ATP molecule
 3 PG → 1,3BPG (via dehydrogenase)
 PEP → Pyruvate (via pyruvate kinase)
- Glycolysis is regulated at 3 steps involving non-equilibrium reactions. These reactions are catalyzed by
 1. Hexokinase (and glucokinase)
 2. Phosphofructokinase
 3. Pyruvate kinase
- Phosphofructokinase -1 (PFK-1) catalyzes the committed step of glycolysis.
- In RBCs (erythrocyte) 1st site of ATP formation i.e. phosphoglycerokinase reaction may be bypassed. However 2,3 BPG is synthesized.

TCA Cycle (Kreb's or Citric Acid Cycle)

- Requires oxygen. Present in virtually all eukaryotic cells that contain mitochondria, but functions only as part of aerobic metabolism (when oxygen is available)
- TCA cycle is the final common pathway of oxidation

of CBH, fats, and proteins through which acetyl CoA is completely oxidised into CO₂ + H₂O

- Only step in TCA where substrate level phosphorylation occur - succinate thiokinase or succinyl CoA synthetase or succinyl CoA ligase



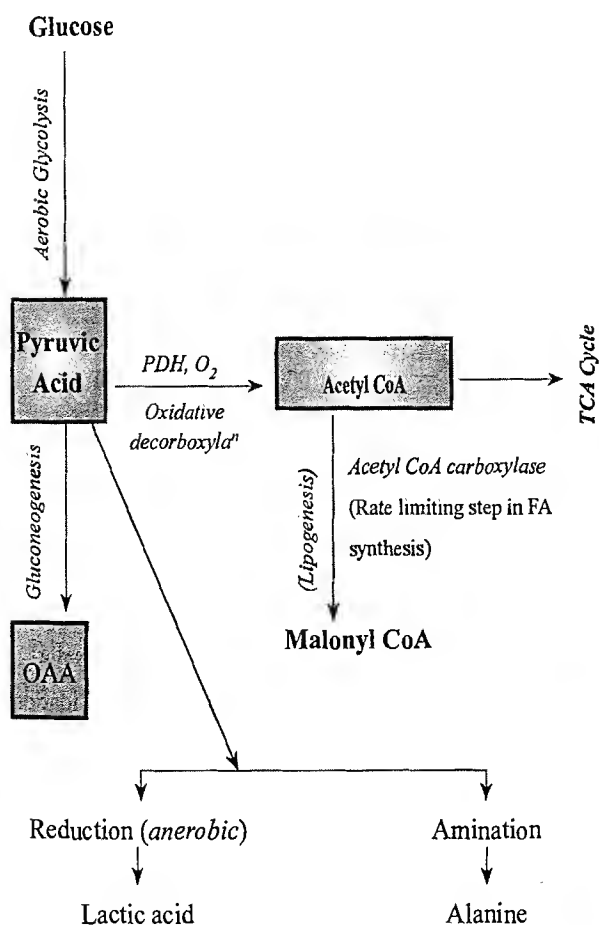
- In TCA — Steps where irreversible reaction occur
 1. Citrate synthase (acetyl CoA + OAA → Citrate)
 2. α-KG dehydrogenase (α-KG → Succinyl CoA)
- Vitamins involved in citric acid cycle are — B1, B2, Niacin & Pantothenic acid.
- Function of citrate in TCA → Activation of acetyl CoA carboxylase.
- Kreb's cycle or citric acid cycle is an amphibolic pathway, meaning that it can be used for both the synthesis and degradation of biomolecules. It serves both catabolic as well as anabolic functions.
- The first reaction of the cycle, in which oxaloacetate (a 4C compound) condenses with acetate (a 2C compound) to form citrate (a six carbon compound) is typically anabolic. The next few reactions, which are intramolecular rearrangements, produce isocitrate.

- The following two reactions are typically catabolic. CO_2 is lost in each step and succinate (a four carbon compound) is produced.

- RBCs (erythrocyte) which lacks mitochondria (O_2 supply) completely reliant on glucose (Aerobic glycolysis) for their metabolic fuel. TCA cycle does not occur in RBC because there is no mitochondria.
- In glycolysis first committed step is catalysed by --- phosphofructokinase
- For estimation of blood glucose fluoride is added to the blood samples. Fluoride inhibits enolase.

Fate of Pyruvic acid

Pyruvic acid is the key substance in phase II metabolism. It is transformed into glucose, lactic acid, OAA, and acetyl CoA.



- The pathway of carbohydrate and fat metabolism meet at the common intermediate acetic acid (Acetyl CoA)
- Acetyl CoA serves as link between glycolysis and TCA cycle
- Fumarate serves as a link b/w urea cycle and citric acid cycle
- UDP-glucose is the key substrate for glycogen synthesis.

ACETYL CoA

- FA, cholesterol (& other steroids), KB (ketones and acetoacetate) can all be synthesized directly from acetyl CoA.
- Acetyl CoA
 - Is common product of carbohydrate, fats & protein metabolism.
 - Is starting material for FA synthesis
 - Serves as link b/w glycolysis & TCA cycle
- Acetyl CoA is also k/as active acetate as its acetyl group combines readily with other substances in reactions that would otherwise require outside energy.
- Acetyl CoA can not be directly converted into
 - Puruvate because it is an irreversible step.
 - Glucose (It is not a substrate for gluconeogenesis)
 - β -OH butyrate

Metabolic pathway in various states

	Fed	Fasting	DM
Anabolism			
	Glycogen synthesis	+	-
	Glycolysis (Liver)	+	-
	TG synthesis	+	-
	FA synthesis	+	-
	Protein synthesis	+	-
Catabolism			
	Cholesterol synthesis	+	-
	Glycogenolysis	-	+
	Gluconeogenesis (Liver)	-	+
	Lipolysis	-	+
	FA oxidation (β -oxidation)	-	+
	Ketogenesis (Liver)	-	+
	Ketone bodies utilization by non hepatic tissues	-	+
	Protein breakdown	-	+/-

[+ means activated or increased and - means suppressed]

- In DM all genesis or synthesis & required enzymes are suppressed (except gluconeogenesis and ketogenesis) and all lysis / catabolic paths are promoted (except glycolysis). Actions of insulin are opposite
- Actions of insulin are similar to metabolism in well fed state (as insulin signals fed state)
- Metabolism is almost similar in fasting state, starvation and DM

INSULIN

- Secreted in response to hyperglycemia & signals fed state. Anabolic activities are stimulated to utilize and divert glucose (Remember - *insulin causes all genesis except gluconeogenesis and ketogenesis*)
- Insulin secretion is ↓ by --- Epinephrine
- Promotes utilization of glucose in muscles, mammary glands, adipose tissues, and myocardium via GLUT-4 [mnemonic: My MAMc] but not in RBCs, WBCs, brain, renal tubules, intestine and liver/hepatocytes (Here glucose is utilized without any insulin requirement or without GLUT)

→ In animals fed with high CBH diet FA oxidation is spared because lipolysis in adipose tissues is inhibited d/to high blood glucose and insulin concentrations & therefore FFA level remains low.

→ Glucagon is released from liver when blood glucose falls i.e. in response to hypoglycemia (between meals, during fasting/starvation) & directs catabolic activities

→ Glucagon excess is a/w hyperglycemia and it can be a feature of glucagonoma or DM

→ Actions of insulin are similar to metabolism in well fed state (as insulin signals fed state)

→ Adrenaline has effects similar to glucagon but more on m/s. It is released during exercise to promote catabolism of glucose & fat (i.e. to ↑ blood glucose level to support muscle activities). Anti insulin hormone.

GLUT (Glucose Transporters)

- GLUTs mediate facilitated diffusion of glucose across cell membranes. GLUT 4 is transporter in muscle and adipose tissue that is mediated by insulin. Reduced in fasting state when insulin levels are low. After a overnight fast level of GLUT receptors is ↓ in adipocytes.
- There are 5 types of GLUT
 - GLUT-1 --- Brain, colon, kidney, placenta, RBCs
 - GLUT-2 --- Liver, pancreatic β- cells, SI, kidney. are freely permeable to glucose via GLUT2
 - GLUT-3 --- in brain, kidney, placenta
 - GLUT-4 --- in heart, skeletal m/s, adipose tissue
 - GLUT-5 --- in small intestine
- SGLT (Sodium Glucose Cotransporters)
 - SGLT-1 --- Found in small intestine, renal tubules
 - SGLT-2 --- Found in renal tubules

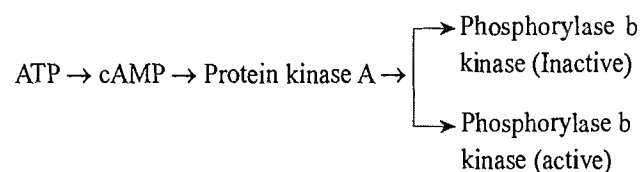
Substrate for gluconeogenesis

- Glycogenic a/a (especially alanine) > lactate, pyruvate, glycerol, propionic a. (which forms propionyl CoA)
- Acetone (one of the KB) can form glucose passively by propanediol-P pathway.
- Acetate can form glucose only by running through the glyoxylate cycle.
- FA & KB can not be used, FA forms acetyl CoA

Glycogenolysis

- In the liver (but not in muscles), the specific enzyme G-6-phosphatase is present which dephosphorylates G-6-P and promotes entry of the glucose into the blood.
- Epinephrine and glucagon promote hepatic glycogenolysis by stimulating adenyl cyclase
- Epinephrine also activates adenyl cyclase in skeletal m/s.
- Glycogen phosphorylase is kept inhibited in liver by free glucose.

Hepatic Glycogenolysis



phosphorylase b → phosphorylase a (active)

Glycogen $\xrightarrow{\text{(glycogenolysis)}}$ G-6-P

Effect of Glucose Feeding

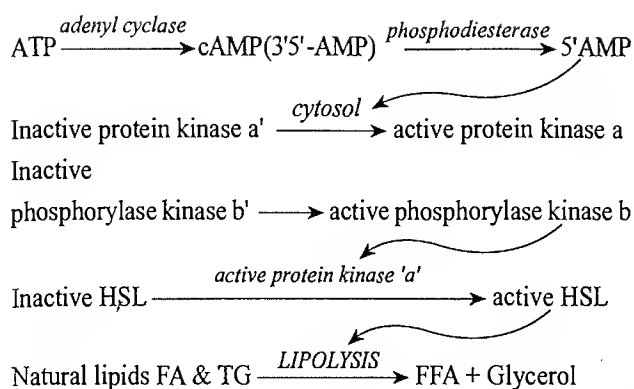
After a meal containing 60 gm carbohydrate or glucose, blood sugar rises by following enzymes

- ↑ ed activity of
 - Enzymes of glycogenesis, glycolysis, pyruvate oxidation (Glycogen synthase, Gluco/hexokinase, phosphofructokinase)
 - Enzymes of PPP and lipogenesis (ATP citrate lyase, FA synthase, Acetyl CoA carboxylase, G-6-PD)
- ↓ ed activity of
 - Enzymes of gluconeogenesis (Pyruvate carboxylase, PEPC kinase, Fructose 1,6 bi phosphatase, G-6-phosphatase)

CYCLIC AMP

Hormones ↑ ing Adenyl Cyclase (and cAMP)

- Epinephrine / adrenaline (↑ in liver & m/s)
- Glucagon (in liver only)
- ACTH (in adrenal cortex)



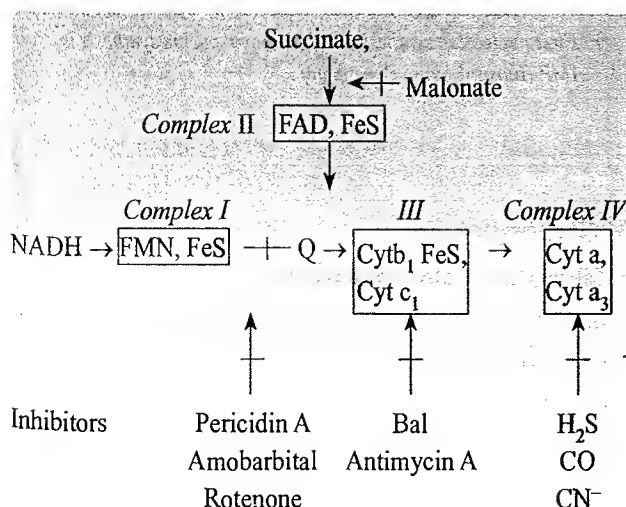
c-AMP activates

- Gluconeogenesis and glycogenolysis (\uparrow blood glucose)
- \uparrow HSL \rightarrow Lipolysis \rightarrow \uparrow FFA level
- Protein synthesis (stimulates transcription & translation)
- \uparrow BMR, \uparrow S.calcium (smooth muscle relaxation & vasodilatation)
- \uparrow HR, \uparrow contractility (cardiac stimulant)

c-AMP Inhibits

- Glycolysis & cholesterol synthesis (\downarrow serum cholesterol level)
- Inactivates glycogen synthetase thus **glycogenesis**
- \rightarrow Hormones acting via c-AMP (by stimulating adenyl cyclase they \uparrow cAMP level) — Adr, NA, glucagon, ACTH, TSH, PTH, Gonadotropins (TSH/FSH), hypothalamic releasing hormones
- \rightarrow Methylxanthines (theophylline > caffeine > theobromine) inhibit phosphodiesterase enzyme thus increase c-AMP level
- \rightarrow Sildenafil (content of Viagra) also inhibits phosphodiesterase & \uparrow c-AMP level (smooth muscle relaxation & vasodilatation)
- \rightarrow Insulin, prostaglandins, stimulate phosphodiesterase thus decreasing cAMP level
- \rightarrow Under physiological conditions phosphorylase b is inactive in skeletal m/s d/to inhibitory effect of — protein phosphatase I

Inhibitors of ETC



- Barbiturates inhibit NAD linked dehydrogenases by blocking the transfer from FeS to Q
- Complex IV is Cyt. C oxidase and contains Cyt a-Cu⁺⁺, Cyt a₃. It is blocked by H₂S, Co, cyanides and azides.
- Antimycin A and BAL (Dimercaprol) inhibits resp. chain b/n Cyt b and Cyt c i.e. complex III.

SOME IMPORTANT INHIBITORS

	Inhibitor	Inhibits
Glycolysis	Arsenic	Phosphoglycerate kinase
	Iodoacetate	Glyceraldehyde-3-P-dehydrogenase
	Fluoride	Enolase
	Citrate, ATP, c-AMP, Glucagon	Phosphofructokinase
Kreb's cycle	Fluoroacetate	Aconitase (fluoroacetyl CoA condenses oxaloacetate to form fluocitrate)
	Arsenic	α -KG dehydrogenase
	Malonate	Succinate dehydrogenase
Oxidative phosphoryla ⁿ	Oligomycin	Blocks flow of protons through ATP synthase
	Atractyloside Bongrakate	Inhibits transport of ADP in & ATP out across mitochondria thus prevents formation of ATP

Uncouplers of oxidative phosphorylation

1. CCCP (most active) :Physiological
2. 2,4 DNP (Dinitro phenol), dicoumarol
3. Calcium, alcohol,
4. Salicylates, cyanides, CO

OXIDATIVE DECORBOXYLATION

- Thiamine, niacin, lipoic acids etc are used.
- Enzymes used in oxidative decarboxylation: PDH (Pyruvate dehydrogenase), Dihydrolipoyl transacetylase, Dihydrolipoyl dehydrogenase
- Their prosthetic group includes: NAD, FAD,TDP,Thiamine diphosphate,acetyl CoA.

Intermediates of Metabolism

- High energy phosphate compounds (Liberate 10-12 Kcal/mol)
These are ATP, ADP, Creatine- PO_4 , DAG, phosphopyruvate, acetyl phosphate
- Low energy phosphates (Liberate 2-3 Kcal/mol)
G-6-P, G-1-P, FDP, AMP, phosphoglyceraldehyde, etc.
- High energy esters
Coenzyme-A (CoA)

Substrate Level Phosphorylation

- In Glycolysis
 $3 \text{ PG} \rightarrow 1,3\text{BPG}$ (via dehydrogenase)
 $\text{PEP} \rightarrow \text{Pyruvate}$ (via pyruvate kinase)
- In Krebs cycle
 $\text{Succinyl CoA} \rightarrow \text{Succinic acid}$ (via succinate thiokinase or succinyl CoA synthetase or succinyl CoA ligase).

→ Enzymes activated in phosphorylated form E3 ubiquitin ligases, Protein kinase B

→ Phosphorylation on serine is the most common.

Rate limiting steps / key enzymes:

Metabolic Pathway	Rate limiting step
Glycolysis	Phosphofructokinase
Glycogenesis	Glycogen synthetase (dephosphorylated form)
Glycogenolysis	Phosphorylase (phosphorylated form)
Gluconeogenesis	Pyruvate carboxylase, PEP-C
Krebs/ TCA cycle	Isocitrate dehydrogenase
Ketone bodies synthesis	HMG CoA synthetase
In cholesterol synthesis	HMG CoA reductase
FA synthesis (lipogenesis)	Acetyl CoA carboxylase
Catecholamines synthesis	Tyrosine hydroxylase
Uric acid synthesis	Xanthine oxidase
Bile acid synthesis	7- α hydroxylase

(PEP-C = Phospho Enol Pyruvate - Carboxykinase)

- Enzyme common to synthesis of cholesterol & ketone bodies --- HMG Co A synthase.

Urea cycle (Krebs Henseleit /Ornithine Cycle)

- Takes place in **liver** (steps 1,2 in mitochondria & steps 3,4,5 in cytosol) because arginase is present only in liver. Arginine carries NH_3 from m/s to liver.
- Arginase is required in the final step of synthesis of urea from arginine
- In kidney it occurs upto arginine (Arginase is absent in kidney). Kidney synthesizes NH_3 from glutamine
- Brain can synthesize urea from citrulline (but ornithine \rightarrow citrulline conversion does not occur)
Brain can convert excess $\text{NH}_3 \rightarrow$ into glutamine
- Fumarate is bi-product
- Carbamoyl phosphate synthase I is rate limiting step
- 3 ATP required in each turn of cycle
- Source of NH_3 in urine ---- urea
- Source of C & N of urea
 - One nitrogen of NH_2 group is derived from NH_4^+ ion
 - Other nitrogen of NH_2 group is provided by aspartate
 - Carbon is provided by HCO_3^- (bi-carbonate)
- In severe liver d/s BUN falls and NH_3 rises. Excess NH_3 may lead to encephalopathy.

End products of

- Purine catabolism \rightarrow Uric acid
- Pyrimidine catabolism \rightarrow β -Alanine & β -Amino isobutyric acid + NH_3
- FA Oxidation \rightarrow Acetyl CoA (propionyl CoA with odd chain FA)
- Glycolysis \rightarrow Pyruvate
- Nucleic acid on hydrolysis \rightarrow Yields base + sugar
DNA on complete hydrolysis \rightarrow A, G, C, T + Deoxy ribose
RNA on complete hydrolysis \rightarrow A, G, C, U + D-ribose
- Alanine (& glutamine) is a major form by which amino acid arrive at the liver from muscle & other tissues
- First nucleotide synthesized by 'de novo' purine synthesis is IMP (Inositol Mono Phosphate)

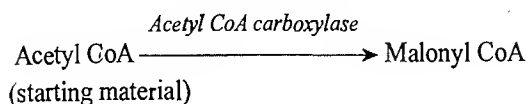
O- Glycosylation

- Takes place in Golgi apparatus.
- Involves a battery of membrane-bound glycoprotein glycosyl transferases.
- Occurs post-translationally at certain serine and threonine residue.

METABOLISM OF LIPIDS/FATS

FA Synthesis (De-novo lipogenesis)

- Occurs in cytosol.
- Rate limiting step is Acetyl CoA carboxylase



- NADPH is utilised (derived from HMP)
- Promoted by Insulin, citrate, high CBH diet, fat free diet
- Inhibited by Palmitoyl CoA, c-AMP, Glucagon
- Carnitine transports acetyl CoA for FA synthesis

TG Synthesis and breakdown

Synthesis of TG (esterification)	Breakdown of TG (lipolysis)
<ul style="list-style-type: none"> Acyl CoA + α-Glycerol-P \rightarrow TG (neutral fat) <p>Promoted by</p> <ul style="list-style-type: none"> Insulin PRL 	$\text{TG} \xrightarrow{\text{HSL}} \text{FFA} + \text{Glycerol}$ <p>\uparrow by \downarrow by</p> <ul style="list-style-type: none"> Adr, NA Glucagon GH Glucocorticoids Acth, MSH, TSH Vassopressin

CHOLESTEROL SYNTHESIS

- Rate limiting step is **HMG-CoA reductase**.
- $$\text{HMG CoA} \xrightarrow{\text{HMG CoA reductase}} \text{Mevalonate}$$
- Promoted by Insulin, thyroid hormones
 - Inhibited by c-AMP, glucagon, glucocorticoid.
 - Cholesterol structurally belongs to steroid. It is a precursor of bile acids, sex steroids, corticosteroids, and vit. D
- Acetoacetyl CoA is the starting material and HMG CoA synthetase is rate limiting step for K.B.synthesis.
- Active FA \rightarrow Acyl CoA
- Active Acetate \rightarrow Acetyl CoA
- FA are not freely permeable across mitochondrial membrane (require carnitine transporter)
- Acetyl CoA is the starting material for the synthesis of long chain FA.

Fatty Acid Oxidation

- Function of citrate in FA oxidation is activation of allosteric enzyme acetyl CoA. Citrate \uparrow es in the well fed state and is an indicator of plentiful supply of acetyl CoA.
- Defect in β - oxidation of FA leads to hypoglycemia.

β -oxidation	α -oxidation	ω -oxidation
<ul style="list-style-type: none"> Oxidation in mitochondria Final product is 2 Carbon less FA with even chain fatty acid FFA \rightarrow acyl CoA \rightarrow acetyl CoA with odd chain FA product is \downarrow propionyl CoA 	<ul style="list-style-type: none"> In brain & liver microsomes Product 'Even' C long chain FA converted to \downarrow Odd chain FA with 1C less Defect-refsum ds 	<ul style="list-style-type: none"> In liver microsomes Product Medium & long chain FA \downarrow di-carboxylic acids

- α & ω oxidation are alternative pathways for oxidation of FA in which no initial activation is necessary & mono oxygenase are required
- Peroxisomal oxidation is oxidation of very long chain FA. Zellweger (hepatorenal) syndrome is d/to defect in this pathway

Fatty Acids

- The presence of double bonds in a molecule classifies that molecule as being unsaturated.

Category	Formula	No. of 'C' atom	Example	Importance
SFA	$\text{C}_n \text{H}_{2n+1} \text{COOH}$	3	Butyric	
		16	Palmitic	
		18	Stearic	
		<10	Lower FA	
MUFA	$\text{C}_n \text{H}_{2n-1} \text{COOH}$	$\omega : 9$	Oleic	
			Elaidic	
PUFA	$\text{C}_{18}\text{H}_{32}\text{O}_2$	18	Linoleic	Most important EFA
	$\omega : 6$			
	$\text{C}_n \text{H}_{2n-3} \text{COOH}$	18	Linolenic	
	$\text{C}_n \text{H}_{2n-1} \text{COOH}$		Arachidonic	Most unsaturated

- Docosahexanoic acid ($\omega : 3$) is synthesized from a linoleic acid. It is required for development of brain and retina and is supplied via milk and placenta.
- Omega -3 ($\omega : 3$) fatty acids have cardioprotective effect.
- The EFA which can synthesize another EFA is linoleic acid. Thus Linoleic acid is the most important EFA.

LIPOPROTEINS

- As the VLDL is the main transporter of endogenous TG, all the conditions ↑ing endogenous TG will also ↑ VLDL secretion or release like well fed state, ↑ of FFA, alcohol ingestion, carbohydrate rich diet, insulin.
- FFA in plasma are transported as albumin-FFA complex.
- Chylomicrons are absent in plasma.
- LDL receptors :
LDL (apo b-100,E) receptors are present on liver as well as on extrahepatic tissues. They are present on clathrin coated pits on cell membrane. ↑ in cell cholesterol downregulates the receptors.

- Lipoprotein which does not move in electrophoresis — Chylomicron (least mobility because they have least proteins)
- Max^m concentration of exogenous TG is seen in — chylomicron
- Max^m concentration of endogenous TG is seen in — VLDL
- Major lipoprotein of blood is — LDL (β - lipoprotein)
- Max^m content of cholesterol is seen in — LDL
- Apo B-100 is major lipoprotein of VLDL, IDL & LDL.
- Apolipoprotein (especially LDL) are most strongly a/w coronary heart disease & HDL have protective role.
- Apolipoprotein B has highest predictive value in morbidity of coronary heart disease.

Human Plasma Lipoproteins

	Chylomicron	VLDL	LDL	HDL
Electrophoresis	Found at origin	pre-β (α ₂)	β	α (or α ₁)
Mobility in electric field	Least		Found in beta region	Highest
Apoprotein	Apo β ₄₈	Apo β -100	Apo β- 100	Apo A-I & -II
Origin (synthesis)	Intestine (-nt in serum)	Liver, intestine	in blood from degradation	Liver of VLDL
Size	1000-10,000 Å ⁰ (max ^m)	300-700 Å ⁰ (min ^m)	150-250 Å ⁰	75-100 Å ⁰
Density	<.96 (lowest)			> 1.063 (Max.)
Major lipids	TG (90%)	TG (50%)	Cholesterol (45%)	PL (30%)
Function	Transports exogenous/ dietary TG (intestine → liver)	Transport endogenous TG liver → peripheral tissue	Atherogenic Causes CAD coronary artery d/s (major transporter of cholesterol in bld)	Scavenging action transports cholesterol from peripheral tissue to liver for degradation

Primary Hyperlipoproteinemias Caused by Known Single Gene Mutations

Genetic Disorder	Gene Defect	Lipoproteins	Cl/f	Genetic transmission
1. Lipoprotein lipase deficiency	LPL	Chylomicrons	Eruptive xanthomas, HSM, pancreatitis	AR
2. Familial apolipoprotein C-II deficiency	ApoC-II	Chylomicrons	"-----"	AR
3. Apo A-V deficiency	ApoA-V	Chylomicrons VLDL	"-----"	AD
4. Familial hepatic lipase deficiency	Hepatic lipase	VLDL remnants	Premature atherosclerosis, pancreatitis	AR
5. Familial dysbetalipoproteinemia	apoE	Chylomicron and VLDL remnants	Palmar and tuberoeruptive xanthomas, CHD, PVD	AR
6. Familial hypercholesterolemia (Muller Harbitz d/s)	LDL receptor defect	LDL	Tendon xanthomas, CHD	AD
7. Familial defective apoB-100	apoB-100 (Arg ₃₅₀₀ → Gln)	LDL	"-----"	AD
8. AD hypercholesterolemia	PCSK9	LDL	"-----"	AD
9. AR hypercholesterolemia	ARH	LDL	"-----"	AR
10. Sitosterolemia	ABCG5 or 8	LDL	"-----"	AR

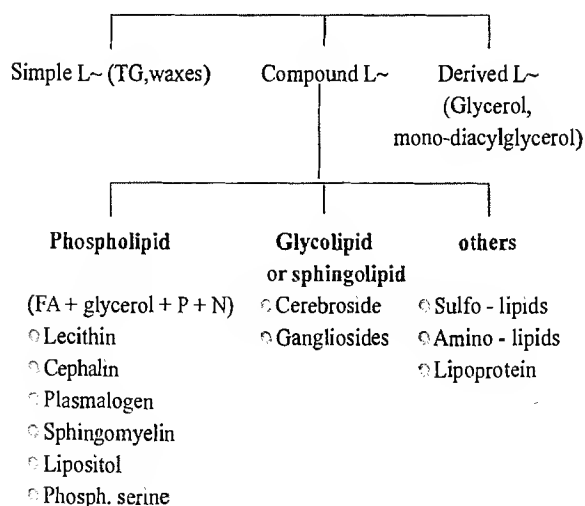
- M/c type is type II i.e. Familial hypercholesterolemia which is d/to — LDL receptor deficiency
- Abetalipoproteinemia is a rare autosomal recessive disorder d/to defective secretion or synthesis of apo-B.
absent or very low level of VLDL, chylomicron, LDL
- Dysbetalipoproteinemia (type III f-) is d/to defect in apo-E which plays crucial role in catabolism of chylomicron and VLDL. Raised level of VLDL, chylomicron remnants, plasma TGs. Tuberous xanthoma are seen.

Apolipoproteins source and function

- Apolipoproteins constitute the protein moiety of lipoproteins.
- They act as enzyme e.g. lipase activators (e.g. apo C-II, and apo A-I) or as ligand for cell receptors (LDL receptor on the liver recognize apo E and apo B 100 ligands).

Apo	Source	Function	a/w lipoprotein
Apo A-I	intestine, liver	Activates LCAT, structural protein for HDL	HDL
Apo B-48	intestine	Structural protein for chylomicrons	chylomicrons
Apo B-100	liver	Structural protein for VLDL, IDL, LDL, ligand for binding to LDL receptor	VLDL, IDL, LDL, Lp(a)
Apo C	liver	Cofactor for lipase	VLDL, HDL, Cm
Apo E	liver	Ligand for binding to LDL receptor	IDL, HDL, Cm remnants

Types of lipids



- All sphingolipids are formed from ceramide
- Examples of sphingolipids are cerebroside & gangliosides
- Fabry's & Krabbe's are sphingolipidoses.
- Glucocerebrosides accumulate in Goucher's & neuroblastoma cells.

Synthesis of brain lipids

- Sphingosine is formed by condensation of palmitic acid with amino-acid serine
Palmitic acid + serine \Rightarrow Sphingosine (or sphingol)
Sphingosine + FA \Rightarrow Ceramide
Ceramide + Glucose \Rightarrow Ceramide-glucose (glucocerebroside)
Ceramide + Phosphocholine \Rightarrow Sphingomyelin
Sphingolipid + Neuraminic acid \Rightarrow ganglioside

- Phosphatides contain glycerol as alcohol group
Cephalin (phosphatidyl ethanolamine)
Lecithin (phosphatidyl choline)
Cardiolipins
Plasmalogens

Enzyme Deficiency in

D/s	Deficient enzyme	Accumulation of
Niemann -Pick	Sphingomyelinase	Sphingomyelin
Tay Sach's	Hexosaminidase A, (Mutations in the HEXA gene)	Ganglioside GM2
Sandhoff's	Hexosaminidase A, B (Defective HEXB gene)	Ganglioside GM2 (Lysosomal storage disorder)
Farber's	Ceraminidase	Ceramide
Fabry's	α - galactosidase A	Sphingolipid Globotriaacylceramide (GL3)
Krabbe's (GM-I ganglio)	β - galactosidase (Lactase)	Galactocerebroside galactosylsphingosine, a sphingolipid
Pompe's (Type II GSD)	α - glucosidase	Glycogen
Goucher's	β - glucosidase (sucrase/maltase)	Glucocerebrosides

Identification of fats and oils

- Saponification number
Amount of detergent required for 100gm of FA. High in short chain FA
- Acid no.
Indicates degree of rancidity of fat
- Iodine no.
Indicates degree of **unsaturation** of fat (ex-iodine no. of linseed oil 175 - 202, olive oil 79 - 88)
- Acetyl no.
Number of OH-group present. Used for detection of adulteration in fat

CARBOHYDRATES

Disaccharides Hydrolysis

Disaccharides on hydrolysis give monosaccharides

- Lactose $\xrightarrow{\text{(lactase)}}$ Glucose + Galactose
- Sucrose $\xrightarrow{\text{(sucrase)}}$ Glucose + Fructose
- (Invertase) \rightarrow L-Glucose + Fructose

- Maltose $\xrightarrow{\text{(maltase)}}$ Glucose + Glucose
- Disaccharidases enzymes are of 2 types
 - β - galactosidase (lactase)
 - α - glucosidases (sucrase, maltase)
- Branching enzyme

Amylo (α -1,4 \rightarrow α -1,6) transglycosylase or Glucosyl α 4:6 transferase. A glycogen branching enzyme is an enzyme that takes part in converting glucose to glycogen
- De-branching enzyme

Oligo (α -1,4 \rightarrow α -1,4) Gluco transferase or Amylo-1 \rightarrow 6 - glucosidase
- Deficiency of α 1-4 glucosidase is seen in Pompe's d/s. Glucosides accumulation is seen (Glucosidosis).

- Lactase deficiency

In response to ingestion of lactose there is bloating, watery diarrhoea, recurrent vague abdominal pain, FTT.
- Sucrase isomaltase deficiency

In response to ingestion of sucrose/glucose containing diet there is bloating, watery diarrhoea, and failure to thrive (FTT) well.
- Hereditary fructose intolerance

In response to ingestion of fruits there is bloating, watery diarrhoea, recurrent vague abdominal pain, FTT.
- Refsum's d/s

Phytanate α -oxidase defect.
- Epimers --- Glucose & Galactose (in C_4), Glucose & Mannose (in C_2)
- Enantiomer --- Optically active pure isomer

- Racemers --- When equal amount of D & L isomers are present, mixture becomes optically inactive.

Monosaccharides (reducing sugars) & Corresponding sugar alcohols on reduction

- D-Glucose \rightarrow D-sorbitol
- D-Galactose \rightarrow D-dulcitol (\uparrow in galactosemia)
- D-mannose \rightarrow D-mannitol
- D-fructose \rightarrow D-mannitol + D-sorbitol

Muta-rotation +ve in

Aldohexoses, D-Glucose, D-Galactose, D-fructose

Osazone formation +ve in

Fructose, Mannose - sunflower shape, Glucose (needle shape/ bundle of hay), Lactose (cotton ball)

[Sucrose does not form osazone]

\rightarrow Sucrose is a non-reducing sugar (invert sugar); does not form osazone.

There is no free aldehyde or keto group in sucrose

\rightarrow Sucrose is called invert sugar because D-sucrose is broken down into L-glucose & L-fructose by invertase.

BIOCHEMICAL TESTS

Tests on Urine

Test	Used for detection of — in urine
○ Benedict	Reducing substance/ RS
○ Rothera	Ketones (Acetone, β - OH butyrate)
○ Hey's sulfur	Bile salts
○ Fouchet's	Bile pigments (qualitative)

- \rightarrow Ehrlich's aldehyde test is used for urobilinogen & porphobilinogen
- \rightarrow Tests for cholesterol include — Salwoski, Liebermann, Ziemann
- \rightarrow Tests for carbohydrates include — Molish for all sugars, Selwenoff (D-fructose), Fearon's
- \rightarrow Rothera's test is false positive in — presence of other ketones e.g. in PKU
- \rightarrow In Ninhydrin reaction all a/a give blue colour except proline and hydroxy-proline which give yellow colour
- \rightarrow Orthotoluidine test is used for detection of — Chlorine

Tests for Proteins

	Test	Used for detection of
Colour reactions	Xanthoproteic	Aromatic amino acids
	Millon's	Tyrosine
	Sakaguchi	Arginine
	Sullivan	Cysteine & cystine
	Lead-acetate	Cysteine, cystine & methionine
Quantitative assay	Hopkins kole aldehyde reac ⁿ	Tryptophan
	Ninhydrin reaction	Detects number of amino acids
	Fluorescamine	Better, Detects number of amino acids
NH ₂ detec ⁿ	Amide group detection	Von-slyke method, Mass spectrometry
Peptide chain sequencing		Edman's (for N terminal)

MUCOPOLYSACCHARIDES

Mucopolysaccharides

There are two types of MPS --- Acidic and neutral

Major categories	Example	Role
Acidic SO ₄ free	Hyaluronic acid (NAG + D-Glucuronic acid)	Abundant in vitreous humour of eye
Acidic SO ₄ containing	Keratan sulfate	Maintains corneal transparency
	Chondroitin sulfate	Present in cartilage
	Heparin (D-Glucosamine + L-Iduronic acid)	
Neutral	ABO/Rh blood group substances	

MUCOPOLYSACCHAROIDOSIS (Lysosomal storage diseases)

Abbreviations

DS = Dermatan sulfate

KS = Keratan sulfate

HS = Heparan sulfate

CS = Chondroitin sulfate

CC = Corneal clouding

MR = Mental retardation

Types	Syndrome/Disease	CI/F	CC	MR	Urine
I	Hurler's (Gargoylism)	Deficiency of α -L-iduronidase. Normal at birth Later coarse facies, kyphosis, hernias, thick skull, joint stiffness, severe d/s	+	+	DS + HS
IS	Scheie	Milder variety, manifest by school age	+	-	DS
I H/S	Hurler-Scheie	Presents early	+	-	DS
II	Hunter	XR-disorder d/to def. of iduronosulfatase Deafness+	-	-	DS min ^m + HS
III	Sanfilippo	Unsteady gait, dysostosis multiplex	\pm (rare)	+	HS
IV	Morquio	Skeletal dysplasia, short stature, anterior beaking of vertebrae (manifest ~ 1 yr of age)	+	-	KS
V	-	Pectus excavatum	+	-	DS, HS
VI	Maroteaux-Lamy			-	DS
VII	Sly syndrome	Def. of β -glucosidase			CS

GLYCOGEN STORAGE DISORDERS OR GLYCOGENOSIS (GSD)

Type	Name	Deficient enzyme	Features
I	Von Gierke's	Glucose-6-phosphatase	Hypoglycemia which improves with epinephrine, lactic acidosis, ketosis, hyperlipidemia
II	Pompe's (Glucosidosis)	Lysosomal α -1,4-glucosidase (Acid maltase)	Heart failure, fatal
III	Forbes/Cori (Limit dextrinosis)	Debranching enzyme (α -1,6-glucosidase)	
IV	Anderson's (Amylopectinosis)	α -1,4 glucan branching enzyme	Cardiac/liver failure in infancy
V	McArdle	Muscle phosphorylase	$\uparrow\uparrow$ glycogen in muscle, Marked m/s pain/stiffness on exercise
VI	Her's	Hepatic phosphorylase	$\uparrow\uparrow$ glycogen in liver, Hypoglycemia
VII	Tarui's	Phosphofructokinase in muscles/RBCs	Hemolytic anemia + McArdle like (m/s pain/stiffness)

SOME INBORN ERRORS OF METABOLISM (IEM)

IEM	Defective pathway or Clinical features	Deficient enzyme	Urine	Cofactor required in t/t	Dietary advise/ Limiting a/a
Essential pentosuria	Uronic acid pathway → ↑L-xylitol in blood	L-xylitol dehydrogenase	↑L-xylitol		
HFI (hereditary fructose intolerance)		Aldolase-B			
Dibasic amino aciduria	↑Excretion of dibasic amino acids in urine		↑O, L, A		
Cystinuria	Amino acid carrier (transport) defect in renal tubular cells → Malabsorption of amino acids		↑C, O, L, A Cysteine, ornithine, lysine, arginine		
Cystinosis		cystine reductase			
Classical homocystinuria	Cod fish vertebrae, hepatomegaly, osteoporosis, ectopia lentis, Charlie Chaplin gait	Cystathione synthetase	Overflow aminoaciduria	B ₆ & Folic a.	Cystine
Norrum's d/s	Failure of cholesterol esterification	LCAT			
Orotic aciduria	Megaloblastic anemia	OMP decarboxylase			
Alkaptonuria	Deposition of homogentisic acid in joints → arthritis (<i>Ochronosis</i>), of hydroquinone → generalized pigmentation of connective tissues	Homogentisic acid oxidase	Urine is dark on standing in air, the only sign in children		
Phenylketonuria	Phenylalanine → Tyrosine	PA hydroxylase	Mousy/musty odour in urine		Tyrosine rich diet
Albinism	Inherited defect in melanocytes of eye & skin	Tyrosinase			
Tyrosinosis	Tyrosinemia type I	fumaryl aceto acetate hydrolase	Boiled cabbage urine odour		
Maple Syrup Urine d/s (MSUD)	Branched chain (leucine, isoleucine, valine) ketonuria	α-ketoacid dehydrogenase complex	↑L, I, V Burnt sugar odour	B ₁	Restrict BCAA & give high dose thiamine
Hartnup disease		Niacin		Niacin	Tryptophan
Methyl Malonyl acidemia	Ketosis, hypoglycemia, hyperglycemia, hyperammonemia	Methylmalonyl CoA mutase		B ₁₂	Carnitine
Glutaric aciduria		HMG CoA lyase	Sweaty feet odour in urine		
Isovaleric acidemia	Ketoacidosis, hyperglycemia, hyperammonemia	Isovaleryl CoA dehydrogenase	Sweaty feet odour in urine		Glycine, carnitine

→ *Ochronosis* is deposition of homogentisic acid in joints.
 → *Tophi* is deposition of monosodium urate crystals in joints.

→ *Fanconi Bickel syndrome* is a rare AR disorder of carbohydrate metabolism d/to mutations in *GLUT-2 (SLC2 A2 gene)*.

CELL MEMBRANE

Characteristics of Bio-membrane

- Basic or key structure of all membranes is **lipid bilayer**
- Asymmetrie & dynamic structure.
- Hydrophobic regions of the phospholipids are protected from the aqueous environment, while hydrophilic ends are immersed in water. Lipids and certain proteins show rapid lateral diffusion. Phospholipids exhibit very slow 'flip-flop' movements but proteins do not show flip-flop.
- Protein composition differs in membranes. Most membrane proteins c/b separated from one-another using SDS-PAGE.

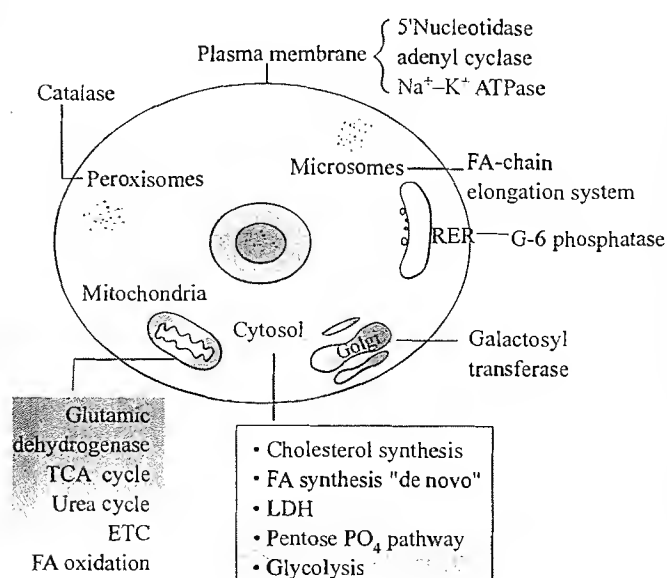
The Fluid Mosaic Model of Membrane

- Proposed by Singer and Nicolson in 1972
- The membrane consist of a bimolecular lipid layer with proteins inserted in it or bound to either surface.
- Integral proteins** are *firmly embedded* in lipid bilayers. Some of these proteins k/as **transmembrane proteins**, completely span the bilayer
Integral proteins have two hydrophilic ends separated by an intervening hydrophobic region (transverse region). They are most abundant, usually globular and are **amphipathic**. They interact with phospholipids (PL) and are asymmetrically distributed across the membrane bilayer.
- Peripheral proteins** are *loosely bound* to membrane. They do not interact with PL directly.
- All the glycolipids and many of the proteins have externally exposed oligosaccharide chains.
- Fluidity of membranes are largely dependent upon the lipid composition of membrane.

Mitchell's hypothesis or Chemio-Osmotic Theory

- Explains how the free energy generated by the electron transport chain is used to provide ATP from ADP + Pi. It links the ATP production and respiratory chain.
- The electro chemical potential difference resulting from the asymmetric distribution of the hydrogen ions is used to drive the mechanism responsible for the formation of ATP.
- Inner mitochondrial membrane is impermeable to ions in general but particularly to protons, the relative impermeability of the inner membrane necessitates exchange transporters.

Markers of various cell organelles



Metabolic processes occurring in various cell organelle

Part of cell		Metabolic /biochemical reactions which takes place, Enzymes which are present
Cytosol		Fatty acid synthesis
		Glycolysis (EMP pathway)
		EMP pathway
Mitochondria	Outer membrane (OMM)	CPT-I, MAO
		Acetyl CoA synthatase
		Phospholipase A ₂
	Intermembrane space	Adenylate kinase, creatinine kinase
	Inner membrane (IMM)	CPT-II
		ETC /respiratory chain
Matrix		ATP synthase
		Oxidative phosphorylation, KB synthesis
		β-oxidation of FA
		TCA cycle, urea cycle
		Alcohol dehydrogenase, PDH, SGOT
In both mitochondria + cytosol		Urea cycle (1st 2 steps)
		Gluconeogenesis

[Carnitine Palmatyl Transferase = CPT]

- Inner membrane is freely permeable to unchanged small molecules e.g. O_2 , H_2O , CO_2 , NH_3 , monocarboxylic acids
- Transporters are required to cross inner mitochondrial membrane—for long chain FA, NADPH, ATP/ADP
- Creatinine kinase is an enzyme of intermembrane space
- Biological oxidation takes place in outer membrane of mitochondria.

- **Cytoplasmic Enzymes** : FA synthase, LDH, Enzymes of glycolysis, PPP
- **Golgi body Enzymes** : GlcNAC transferase I (cis), Galactosyl transferase (for trans Golgi)
- **Lysosomal Enzymes** : Cathepsin

RED CELLS (RBCS)

Biochemical Functions of Mature RBC

- Anaerobic glycolysis (End product is lactate)
- Pentose phosphate shunt (synthesis of glutathione and NADPH)
- Methemoglobin reductase system (reduces heme iron from Fe^{+++} to Fe^{++})
- Synthesis of 2, 3-DPG (causes right shift of ODC), G-6-P

RBC Metabolism

- RBC is highly dependent on glucose as its energy source. Membrane contains high affinity glucose transporters.
- As there is no mitochondria there is no production of ATP by oxidative phosphorylation. Only anaerobic glycolysis is possible, which produces lactate & ATP.

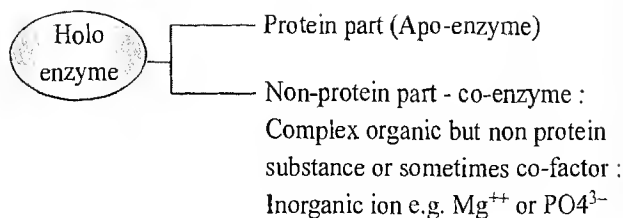
→ RBCs lack mitochondria (so no Krebs cycle in RBCs), nuclei and class-I and II HLA antigens.

→ Synthesis of glycogen, fatty acids, protein and nucleic acids do not occur in RBCs.

ENZYMES

Holoenzyme

- A holoenzyme is composed of an apoenzyme + prosthetic group
- An apoenzyme is a protein part
- A prosthetic group may be either coenzyme or co-factor but not protein substance



Co-factor

A Cofactor is an inorganic ion e.g. Mg^{++} or PO_4^{3-}

Isoenzymes or Isozymes

Many enzymes have several physically distinct versions, each of which catalyzes the same reaction, k/as isoenzymes. Isoenzymes are protein catalysts.

Abenzymes

Abenzymes are antibodies with catalytic activities

Properties of Enzymes

- V_{max} is not altered by competitive inhibitor
- Enzyme cascade reaction is subjected to feed back inhibition.
- Do not alter the equilibrium constant of reaction that they catalyze.
- Enzymes catalyze the reaction by ↓ing the free energy of activation.
- Catalytic property of enzyme is determined by final energy states of the substrate and product (S& P).

Hepatic Microsomal Enzymes

- They are located on smooth ER
- Catalyse most of the oxidation, reduction, conjugation reactions e.g. Cyt. P450, MAO, glucuronyl transferase
- Acts on both exogenous (e.g. various drugs) and endogenous substances
- NADPH and O_2 are required for oxidation reactions carried out by monooxygenases
- All the reactions of metabolism depends upon the catalytic activity of the enzyme system.

Non heme Iron sulphur Protein

Co-enz Q (ubiquinones) present in mitochondria

Fe - porphyrins

Contain heme. Examples are Hb, Cytochromes, Catalase, Peroxidase

- *Allosteric enzyme* --- Phosphofructokinase
- CYP 3A4/5 is the m/c cytochrome involved in biotransformation of largest number of drugs (50%)
- *Suicidal enzyme* --- cyclooxygenase
- RNAs are not proteins but can act as enzyme (Ribozyme) with catalytic activity.
- Ribonuclease P is a ubiquitous ribonucleoprotein enzyme.

Reversible enzyme inhibition : Types

Type of inhibition	Michaelis constant (Km)	Maximum reaction velocity (V _{max})	Lineweaver Burk-plot
Competitive	↑	Unchanged	slope varies Intercept const.
Uncompetitive	↑	↓	slope const. intercept varies
Non-competitive	Unchanged	↓	slope varies intercept varies

Examples of enzymes

Transferases	<ul style="list-style-type: none"> ◊ Glucokinases ◊ Hexokinases ◊ Phosphoglucosmutase ◊ Transaminases
Oxidoreductases	<ul style="list-style-type: none"> ◊ Dehydrogenases ◊ Xanthine oxidase ◊ Oxygenases ◊ Glutathione reductase ◊ Tyrosinase
Hydrolase	<ul style="list-style-type: none"> ◊ G-6-P ◊ Trypsin ◊ Peptidase
Isomerase	<ul style="list-style-type: none"> ◊ Epimerase ◊ Racemase
Ligase	<ul style="list-style-type: none"> ◊ Synthetases ◊ Corboxylase
Lyase	<ul style="list-style-type: none"> ◊ Arginosuccinase ◊ Fumarase ◊ Aldolase

- *Oxidation reduction reactions occur with* --- hydroperoxidases, oxidases, dehydrogenases etc.
- *Transferases are enzymes that catalyze the transfer of functional group from one molecule to another.* Transformation of aminoacids to ketoacids is done by transaminases (aminotransferases)
- NAD is the m/c coenzyme acceptor for dehydrogenation reaction.

Enzymes induced in DM & Fasting

These are enzymes which are induced whenever there is low insulin : glucagon ratio

1. Glucose - 6-phosphatase
2. PePCK (Phospho enol Pyruvate Carboxy Kinase)
3. Pyruvate corboxylase

Enzymes suppressed (↓ activity) in Fasting & DM

1. Glycogen synthase
2. Citrate synthase (key enzymes of gluconeogenesis)
3. Phospho fructokinase -I
4. Hexokinase/ glucokinase
5. Pyruvate kinase (L- isozyme)
6. Pyruvate dehydrogenase
7. Acetyl CoA corboxylase
8. HMG CoA reductase

PEPTIDASES

Peptidases	Example	
Exopeptidases	Carboxy peptidase A & B, amino peptidase, prolidase	Cleaves amino acids at terminal
Endopeptidases (Serine protease)	Elastase, trypsin, chymotrypsin, collagenase	Cleaves amino acids of peptide chain in the middle

DETOXIFICATION/XENOBIOTICS

- ◊ Process by which toxic/harmful molecules (Drugs, food additives, pollutants, carcinogens etc.) of the body are converted into non-toxic /less harmful substances.
- ◊ *Benzoic acid* is metabolized by → conjugating it by glycine or by glycuronic acid.
- ◊ Liver is the principal site of detoxification of drugs.
- ◊ Conjugation with D-Glucuronic acid is the m/c & most important detoxification reaction. Enzyme required is Glucuronic transferase.
- ◊ INH (Isoniazid) is detoxified by acetylation.
- ◊ Histamine & nicotinamide are metabolised by methylation.

- Natural estrogens, epinephrine & NE are metabolised by O-Methylation.
- Phenol, cresol, indole are conjugated with sulfuric acids to form etheral sulfates which are excreted in urine. Active sulfate is chemically PAPS (3-phospho adenosine-5'-phospho sulfate).
 - Some drugs & carcinogens are detoxified by conjugation with glutathione (G-SH), which is catalyzed by glutathione-S transferases.
 - Conjugation with D-Glucuronic acid is employed for detoxification of:
 - Bilirubin
 - Benzoic acid & other aromatic acids
 - Phenol, pyridine, chloramphenicol (Compounds with cyclic ring)
 - Thyroid hormones, steroid derivatives
 - Most of the drugs (>50%) are detoxified by hydroxylation. Enzymes utilised are: monooxygenases or cytochrome P 450.
 - Cytochrome P-450 system:
 - An inducible enzyme present in ER & liver microsomes
 - Chemically haeme-proteins
 - Enzyme require is NADPH - cyt p-450 reductase.
 - BAL detoxifies war poisons /heavy metals like As, gold, Hg, Cd.

HEMOGLOBIN (HB)

- Hb is a conjugated allosteric protein (Quaternary structure), protein part is globin and pigment is heme.
- Hb is a Iron-porphyrin compound (Porphyrins are compound with tetra-pyrrole structure). 4 Pyrrole are combined with methyne/methyldiene bridges
- Heme in Hb is present in "Hydrophobic pockets". Iron in heme is in Fe^{++} form, which is bound to histidine and 4 pyrroles. Globin chain consist of **His, Arg, Lys** amino acids [Mnemonic : Hi- Argily].
- Slowest enzyme in heme synthesis --- ALA synthase.

Properties	Oxy-Hb (HbO)	Reduced-Hb (HbH)
Peak absorption	More infrared light (940 nm)	Absorbs more red light (660 nm)
Wavelength	940 nm	660 nm
Iron in	Fe^{++} (Ferrous form)	Fe^{++} (Ferrous form)

- Iron remains in the "Ferrous" (Fe^{++}) State in both Oxy-Hb and reduced hemoglobin (de-oxygenated Hb). But in Met-Hb, Ferritin, transferrin iron is in "Ferric" (Fe^{+++}) form.

Met-Hb (methemoglobin) is ineffective in oxygen transport.

Concentration of various types of Hb

Type	Embryonic Hb ($\alpha_2\epsilon_2$)	Hb-F ($\alpha_2\gamma_2$)	Hb-A ($\alpha_2\beta_2$)	Hb-A ₂ ($\alpha_2\delta_2$)
First fetal appearance in IUL	4-8 wks (Earliest)	>8 wks	16 wks	30 wks
6 mo IUL	-	90%	5-10%	50%
At birth	-	70%	30%	<1%
2 mo.	-	50%	50%	
12 mo	-	<2%	90-95%	2.3-4%
Adult	-	Disappear	95%	2.4-3.4%

- Switchover or changeover from fetal to adult hemoglobin (HbF to HbA) is probably genetically determined and occurs at around 32 weeks gestational age, regardless of time of birth.
- Beyond infancy, RBCs from patient with HbSS contain 2-20% HbF (increased), with normal level of HbA₂ and HbA is notably -nt.
- Globin chain present in various types of Hb are --- HbA = $\alpha_2\beta_2$, HbA₂ = $\alpha_2\delta_2$, HbF = $\alpha_2\gamma_2$
- If β -chain synthesis does not occur as in β -thal. major there is -nt HbA. If β -chain synthesis \downarrow ed as in β -thal. minor \downarrow ed HbA.
- In patients with β -chain hemoglobinopathies (eg. HbSS, HbSC) HbF level is \uparrow ed.
- Level of HbA₂ \uparrow ed (>3.4%) in β -thal. trait & megaloblastic anemia & \downarrow ed in iron deficiency anemia and α -thalassemia
- Hemoglobin makes its appearance in RBCs in intermediate normoblast stage.
- Nucleus disappears in RBCs in late normoblast stage during erythropoiesis.

Cut off points of Hb for d/g of anemia (WHO)

Age	Anemia			
	Nil	Mild	Mod	Severe
1. Children 6 mo- 59 mo (6 mo - 5 yr), pregnant female	≥ 11	10-10.9	7-9.9	<7 gm%
2. Children 5-11 yr	≥ 11.5	11-11.4	8-10.9	<8 gm%
3. Children 12-14 yr	≥ 12	11-11.9	8-10.9	<8 gm%
4. Non pregnant women (15 yr or +)	≥ 12	11-11.9	8-10.9	<8 gm%
5. Men (15 yr or +)	≥ 13	11-12.9	8-10.9	<8 gm%

- A hemoglobin level of 10-11g/dl has been defined as early anemia & a level below 10g/dl as marked anemia
- Normal Hb level in newborn :- 16 - 18 gm% (newborn is called anemic if Hb level <13 gm% in a sick newborn and <8 gm% in a clinically stable newborn).
- 1 gm of Hb can maximally bind - 1.34 ml of O₂
- 1 gm of Hb contains - 3.34 mg of Iron
- Arterial oxygen tension is almost 100% at 90-100 mmHg in adults and 70-80 mmHg in newborn.
- At an O₂ tension of ≥100 mmHg Hb is virtually 100% saturated.

Diff. between Hb-F & Hb-A

- HbF binds O₂ more avidly than does HbA & tends to shift the ODC curve to the left.
- As a result P₅₀ is decreased (it favours O₂ uptake at the low O₂ tensions in placenta)
- During the first month after the birth ODC begins to shift to the right & between 4 to 6 months of age it is similar to that of adult.
- HbF has low iron content & large size RBC
- HbF is resistant to alkali denaturation. **HbF has least affinity for 2,3 BPG**

- Non-heme iron is present in foods of vegetable origin like legumes, nuts, green leafy vgs, jaggery etc. Iron is in ferric (Fe⁺⁺⁺) form.
- Foods rich in heme iron are liver, meat, poultry & fish. Iron is in ferrous (Fe⁺⁺) form, better for absorption.
- All cytochromes are dehydrogenases except cytoxidases.
- Large amounts of iron inhibitors are present in vegetarian foods — like phytate in bran, phosphate in egg yolk, tannin in tea and oxalates in vegetables.

Myoglobin Vs. Hemoglobin

Myoglobin (Mb)	Hb
○ It binds with 1 mol of O ₂ per mol (monomeric)	○ It binds with 4 mol of O ₂ (tetrameric)
○ It dissociation curve is <u>rectangular hyperbola</u>	○ Sigmoid shape (O ₂ binding is co-operative)
○ Its curve is left to the Hb	
○ It takes up O ₂ from Hb in blood (O ₂ affinity is more than Hb)	○ O ₂ affinity is less than Mb
○ No Bohr effect	○ Hill's co-efficient 2.8
○ Hill's co-efficient is 1.0	

- **Biochemical cooperativity of Hb** : Oxygenation of one heme molecule enhances and accelerates oxygenation of other heme molecules. Similarly the release of one O₂ molecule promotes the release of other this is k/as positive cooperativity and is responsible for sigmoid shaped ODC of Hb.

VITAMINS

Dermatitis is seen with deficiency of :

- Pyridoxine (seborrheic)
- Biotin
- B₂, B₃ [But not with B₁ def.]
- Niacin (Photodermatitis)

Dementia is seen in deficiency of :

- Thiamine
- Niacin
- B₁₂ def.

Angular stomatitis is seen in deficiency of :

- Riboflavin
- Niacin
- Pyridoxine or iron

Requirement of Vitamins in Children (RDA):

B ₁ Thiamine	} 0.5-1.5 mg/d (1mg/1000 cal.)
B ₂ Riboflavin	
B ₆ Pyridoxine	
B ₁₂ cyanocobalamin	0.5-1.5µg/d
B ₃ Niacin	5-15mg/d
B ₁₁ folic acid	50-150 µg/d

Tongue changes in vitamin deficiency :

- Riboflavin def. ---- Magenta tongue
- Niacin def. ---- Beefy/ fiery red tongue
- B₁₂ def. ---- Baldness of tongue
- Folic acid def. ---- Painful tongue
- **Water soluble (w/s) vitamins** are --- Vitamin B and C (Rest are fat soluble viz. A,D,E, K)
- Heat stable, light sensitive --- Vit. K & B₂ (Riboflavin)
- Heat labile vitamins --- Vit. C & Folic acid.

- Vit. deficiency in pancreatic insufficiency --- Vit. A
- Milling of rice causes loss of --- Thiamine (Vit. B2 & Protein also). Parboiling (Hot soaking) preserves above vitamins.
- Riboflavin deficiency is almost always a/w pyridoxine deficiency.
- Mild hemolytic anemia is a/w vit. E deficiency.
Deficiency of Vit. E rarely occur in newborn.
- Co-enzyme A synthesis require Vit. B6 & Co-enzyme A is active form of pantothenic Acid.
- Vit. A deficiency causes : Oro-oculogenital syndrome.
- Vitamin which is detrimental in excess (Hypervitaminosis is seen in) --- Vitamin A, D, niacin, pyridoxine
- Vitamin which is not detrimental in excess --- Vitamin C
- Vitamin which is excreted in urine --- Vitamin C
- Vitamins synthesized by intestinal bacteria --- B complex & K

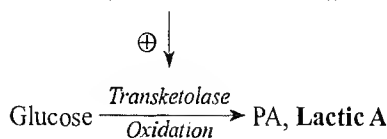
Vitamins required for :

Reaction	
o Carboxylation	Thiamine
o Decarboxylation	Pyridoxine
o Deamination	Riboflavin

Thiamine

- o Essential for carbohydrate utilization, so requirement is related to **carbohydrate** content of diet. Thiamine deficiency causes ↓ energy production

Cocarcboxylase (TPP containing)



- o Required for coboxylation reactions.
- o TPP is a cofactor /coenzyme for 3 multi enzymes which catalyze oxidative decarboxylation reactions:
 - Pyruvate dehydrogenase
 - α-KG dehydrogenase (of α - ketoacids)
 - Pyruvate decarboxylase uses TPP +Mg²⁺
 - Also for transketolase in HMP pathway.
- o Deficiency is
 - Seen in --- alcoholics, chronic diarrhoea, food faddists
 - Diagnosed by --- ↓ **RBC transketolase activity** in blood which improves after adding TPP
 - A/w **lactic acidosis** and pyruvate accumulation
- o The main deficiency d/s are Beriberi and Wernicke -

Korsakoff Syndrome (WKS)

[In WKS, encephalopathy responds to thiamine, but the psychosis usually does not]

- o Used in the t/t of hangover.

Riboflavin

- o FMN & FAD acts as Co-enzyme for various **H-transfer reactions** (electron transfer chain) + **Deamination**.
- o Aqueous solution is unstable in visible and UV-light (**light sensitive** vitamin). Its deficiency may occur in infants under phototherapy.
- o Requirement is related to protein content of diet. Its def. usually occurs in children on restricted proteins intakes or with dominant protein malabsorption state.
- o Co Enzymes :

FMN	FAD
o Warburg's yellow enzyme	o Xanthine oxidase
o Cytochrome-C-reductase	o Aldehyde oxidase
o L-amino oxidase	o Glycine oxidase
	o D-amino oxidase
	o Fumarate deh., Acyl CoA deh
	o Diaphorase

- o Def. causes magenta red tongue, angular stomatitis, cheilosis (fissuring of lips), atrophic glossitis, *neovascularization of cornea*
- o To diagnose its deficiency : ↓ **RBC glutathione reductase activity** ↓.

Niacin (Nicotinic acid)

- o Deficiency occurs in children receiving a **maize** diet as staple diet or other pelagragenic diet like corn, jowar d/to excess leucine). Deficiency also occur in chronic diarrhea, anorexic states, carcinoid syndrome.
- o Synthesized from Tryptophan (60 mg → 1 mg). **Xanthurenic index** is used for tryptophan.
- o Deficiency is assessed by *Konig reaction*
- o Requirement increases in *Hartnup disease* and *Schizophrenia*
- o Def : Raw beef tongue (red and sore tongue).
- o Deficiency may cause Pellagra (**triad** of 3 'D' photo **Dermatitis Diarrhea and Dementia**). Casals necklace glove and stocking type of dermatitis can occur in the exposed areas.
- o Niacin has relaxing effect on anxiety and it is called nature's valium. Tryptophan is called provitamin B₃ and being the precursor of serotonin, it is called nature's 'sleeping pill.'

Pantothenic Acid

- It is a constituent of Coenz. A (Active form of P~ is coenz A)
- Formation of Active acetate (Acetyl Co A), active succinate (Succinyl Co A) - role in heme synthesis, β -oxidation, FA synthesis, steroid synthesis
- Def \rightarrow Burning feet syndrome, Alopecia.

Pyridoxine (Vitamin B₆)

- Deficiency of nutritional origin is rare in childhood deficiency may occur after **prolonged INH or cycloserine therapy in TB or penicillamine therapy in Wilson's disease.**
- Other drugs causing B₆ deficiency : L-dopa, OVP's, carbonyl reagents, alcoholism.
- Pyridoxal-P acts as a conenz for :
 - Transaminases (SGOT & SGPT)
 - Decarboxylation
 - Deamination
- Involved in metabolism of sulphur containing a.a and protein and fatty acids.
- Xanthurenic index to measure deficiency (\uparrow Kynurenine also)
- Pyridoxine dependent inborn errors of metabolism are reported - Homocystinuria, Cystathioninuria, Xanthurenic aciduria, Kynureninase def., hyperoxaluria (PK-CHOX)
- Also role in synthesis of coenzyme A from pantothenic a., synthesis of niacin from tryptophan (60mg \rightarrow 1mg), in synthesis of heme precursor (δ -ALA) and melanin
- For confirmation of D/g : tryptophan loading test.
- Cl/F of deficiency : **Convulsions** and microcytic hypochromic anemia refractory to iron therapy (sideroblastic anemia). Pyridoxine deficiency is a/w neonatal seizures.

Biotin : (Vitamin H)

- Role in CO₂ - fixation reactions (Co-enzyme for **carboxylase**)
- Deficiency causes - Leiner's disease, dermatitis, spectacle eye alopecia in experimental animals.
- Avidin present in raw egg is the **antagonist** of Biotin

Vitamin B₁₂ and Folic Acid

- Intrinsic factor of Castle helps in absorption of vitamin B₁₂.
- B₁₂ deficiency is a/w centrocecal scotoma, megaloblastic anemia.

- Dietary deficiency of Vit B₁₂ is classically seen in vegetarians.
- Castle's d/s is pernicious anemia, a genetically determined condition in which the person is unable to absorb vitamin B₁₂ d/to specific gastric atrophy & loss of IF necessary for its absorption.

Features	Cobalamin/Vit B ₁₂	Folic Acid (vitamin M)
K/as	Extrinsic factor of castle, RBC maturation factor	Acts as one-carbon moiety donor
Present in	Animal diet (Vegetarian diet is deficient in B ₁₂)	Animal diet
Coenzyme for	Homocysteine methyl transferase	
Deficiency assessed by :	<u>Methyl malonyl aciduria index</u>	FIGLU test
CNS effects	+ nt (SACD of spinal cord)	-
Test	Schilling test for \downarrow absorption	Histidine load test.

- Folic acid is advised in early pregnancy to prevent fetal NTDs (neural tube defects).
- Amino acid used for transfer of one carbon moiety --- Methionine, homocysteine.

- \rightarrow Vitamin B₁₂ deficiency causes : Pernicious anemia
- \rightarrow Folate deficiency causes : Megaloblastic anemia
- \rightarrow Deficiency of B₁₂ leads to functional folate deficiency and affects rapidly dividing cells because they have a large reqt. of thymidine for DNA synthesis. Clinically, it affects BM, leading to megaloblastic anemia
- \rightarrow T/t of megaloblastic anemia concurrently with vitamin B₁₂ and folic acid is advised because --- t/t with folates alone may improve megaloblastic anemia but lead to progression of neurological d/s
- \rightarrow Vitamin B₁₂ dependent enzymes are --- Methylmalonyl CoA mutase, leucine aminomutase, methionine synthase
- \rightarrow Folate supplementation reduces the risk of neural tube defects and hyperhomocysteinemia (and thus it indirectly may \downarrow es the incidence of atherosclerosis, thrombosis, and hypertension)

Vitamin C

- Most heat labile vitamin
- \downarrow LDL (Anti-atherogenic)
- Acts as strong **reducing agent**
- It is involved in **collagen synthesis** and bone and teeth formation, formation of hydroxyproline, oxidation of tyrosine and phenylalanine, maintaining integrity of ground

substance and in *hemopoiesis*.

- Local concentration - Pituitary gland > Adrenal cortex > Corpus Luteum
- Def. causes **infantile scurvy** (gross irritability, excess crying, frog position and pseudoparalysis).
- Required for hydroxylation of procollagen in collagen synthesis.

AA' residue + Ascorbic acid + α -Ketoglutarate + O_2

Dioxygenases, Lysyl
or prolylhydroxylase

Fe^{2+}

Hydroxyl AA + Succinate

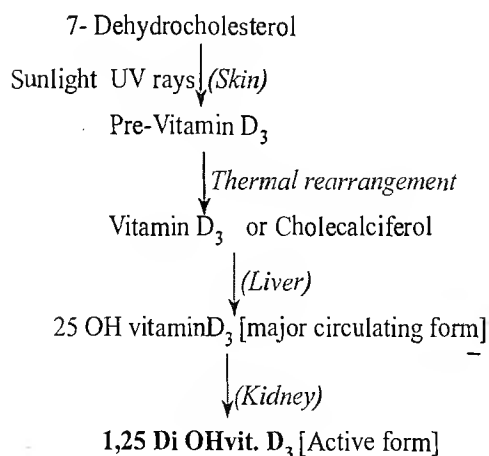
Vitamin E (Tocopherol)

- Heat Labile
- \uparrow HDL (Anti-neoplastic)
- Most important anti-oxidant** (due to chromane ring) in the body
- Free radical scavenger and helps in integrity of cell membrane.
- Deficiency causes - Muscle dystrophies, nocturnal muscle cramps, creatinuria, intermittent claudication, fibrocystic breast disease.
- Vitamin E in excess may lead to NEC in the newborn.
- In neonates deficiency causes mild hemolysis and ataxia.
- Due to its antioxidant property, it is used for prevention and t/t of retinopathy of prematurity, broncho pulmonary dysplasia, hemolytic anemia of prematurity, myopathies, neuromuscular diseases, thrombosis, fibroadenosis etc. prematurity
- Vit. E may be able to slow down the progression of HIV infection to AIDS.*

Vitamin D

- Richest source is Halibut liver oil.
- Cholecalciferol is the animal source and ergosterol (D2) is the plant source.
- Previtamin D3 is synthesized nonenzymatically in the skin (stratum basale & stratum spinosum layers of epidermis) from 7-dhydrocholesterol during exposure to the UV-B rays in sunlight.
- Vitamin D is converted to 25-hydroxyvitamin D (calcidiol), the major circulating form of vitamin D in the liver, and then to 1,25-dihydroxyvitamin D3 (calcitriol) the active form of vitamin D, by the enzymes of in proximal tubular cells of kidney.

The metabolic pathway of Vitamin D:



- Synthetic **vitamin D₂ (ergocalciferol)** is used for fortification of food in milk, infant formula, breakfast cereals in the US.
- Daily requirement in children and infants is 200 IU (5 mcg), pregnancy and lactation is 400 IU (10 mcg), and in adults it is 100 IU (2.5 mcg).
- Deficiency is treated with 6 lakhs IU of vitamin D oral or IM. Now a days weekly oral doses of 60,000 IU for 6-12 weeks are preferred.

Vitamin A

- Retinal is a component of the visual pigment rhodopsin.
- Visual activity of Rod cells is dependent on their content of photosensitive pigment called "Rhodopsin" or **visual purple**. Rhodopsin, occurs in the rod cells of retina which are responsible for vision in poor light.

Rhodopsin = Opsin + Retinene
(conjugated protein) (apoprotein) (Prosthetic gp.)

- 11-Cis-retinal, an isomer of all trans-retinal is specifically bound to the visual protein opsin to form rhodopsin.

Rhodopsin $\xrightarrow[\text{COMP}]{\text{light}}$ all-trans-retinal + opsin

- In the **dark** phase, 11-Cis-retinal exists with opsin.
- In the **light** phase, 11-trans-retinal exists with opsin.
- Dopamine (DA) and acetylcholine (Ach) are neurotransmitters that are present in the visual pathway.* DA is present in the retina and is a/w the interplexiform cells and horizontal cells. Ach is also present in the retina and is a/w displaced amacrine cells; it is also present in the superior colliculus.
- About 95% of vitamin A is stored as its ester (retinal) mainly as palmitate in the liver. It is released in the

plasma as and when required. Aprox. 10-20 mg of vitamin A is present per 100 gm of liver.

- Daily requirement of vitamin A is 600 µg in adults and 350 µg in infants.
- Overdose of vitamin A causes injury to lysosomes.

- Normal blood level of vitamin A is 18-60 µg/dl
- All-trans retinoic acid (Tretinoin) is used topically, while 13-cis retinoic acid (Isotretinoin) is given orally for acne
- Retinol and retinoic acid are included in steroid receptor supergene family hormones.
- β-Carotene (like vitamin D) is a prohormone
- Both retinoids and carotenoids have anti-cancer activity
- Vitamin A overdose causes injury to lysosomes.

Vitamin K

- Vitamin K epoxide cycle is seen in gamma carboxylation of bone gla protein.
- Prophylactic dose in newborn to prevent HDN is vitamin K₁ 1 mg i/m in anterolateral thigh.

MINERALS

Micronutrients/ Microminerals/ Trace elements

Daily requirement is <100 mg/d

Essential

Iron, Cu, iodine, Mn, Zn, Mo, Co, F, Se, and Chromium

Possibly essential

Nickel, Va, Cd, Ba

Non-essential

Al, lead, Hg, boron, Ag, Bi

Macronutrients/ Macrominerals

Daily requirement is >100 mg/d. They constitute 60-80% of the body's inorganic material. These are

Ca, P, Mg, S, K⁺, Cl⁻

Commonest Cl/f of Micronutrient Deficiency

- Zn ---- Perioral pustular rash
- Cu ---- Microcytic anemia
- Cr ---- Hyperglycemia
- Mn ---- Dermatitis

Thyroid disorders a/w micronutrient excess or deficiency

	Hypothyroidism	Hyperthyroidism
Zn	↑	↓
Cu	-	↑
Se	↓	↓

Selenium

- Cofactor for Glutathione peroxidase
- Found to prevent Liver cell necrosis
- Deficiency causes Keshan's disease and Kaschinbeck disease
- Rich in garlic
- Anti-oxidant and anti-cancer property. Deficiency is known to produce atherosclerosis, and tumorigenesis

Zinc (Zn)

- Deficiency causes : Acrodermatitis enteropathica, impaired spermatogenesis, hypogonadism, dwarfism
- Excess causes : Anemia, ARDS, pulmonary fibrosis

Copper (Cu)

- Present in blood, combines with α-globulin and forms ceruloplasmin
- Deficiency causes : Growth retardation, refractory hypochromic anemia, neutropenia, subperiosteal hematoma, osteoporosis, hypercholesterolemia
- Excess causes : Fanconi like syndrome, hemolytic anemia.
- Inherited disorders of Cu. metabolism :
Wilson's disease --
Menke's disease -- Sex linked-R neurodegenerative disorder due to Cu-deficiency (Kinky/steel hair syndrome)

Chromium (Cr.)

- Also called "Glucose tolerance factor"
- Potentiator of insulin
- Deficiency causes DM like picture: hyperglycemia, glycosuria, peripheral neuropathy, encephalopathy.

→ Se-deficiency, Cobalt-excess & iron excess causes --- cardiomyopathy.

→ Se-deficiency causes hypothyroidism as it is required for the enzyme de-iodinase as a cofactor.

→ Mn Toxicity is a/w → Parkinsonism

→ Al deficiency is a/w → Alzheimer's disease

→ Cd deficiency leads to --- Ouch-Ouch disease

→ As & Thallium : Black foot d/s

Mineral	Cofactor in	Other role	Deficiency
Cu	Cytochrome oxidase, MAO, ascorbic acid oxidase, catalase, tyrosinase, lysyl oxidase, dopamine hydroxylase	Combines with α globulin & forms ceruloplasmin	Refractory hypochromic anemia, neutropenia, osteoporosis, growth, Wilson's d/s, Menke's d/s, Kinky hair d/s
Zn	Carboxy peptidase, Carbonic anhydrase, Insulin, ALP, Retinol reductase, Alcohol dehydrogenase	Max ^m concentr ⁿ in prostate. Also found in brain, m/s, bone & kidney	Acrodermatitis enteropathica, hypogonadism, Dwarfism
Mo	Xanthine oxidase, Aldehyde oxidase	Utilization of Cu, Role in uric acid metabolism	
Mn	Pyruvate carboxylase	Lipotropic effect	
Mg ⁺⁺	Kinases, phosphatase (Phosphorylation & dephosphorylation), ribonuclease, adenyl cyclase & transketolase	—	
Se	Glutathione peroxidase	Prevents liver cell necrosis, rich in garlic	Keshan's d/s, Kaschinbeck d/s
Cr	Glucose tolerance factor	Potentiator of insulin	DM like syndrome

HORMONES

Chemical nature of hormones

- Glycoproteins - TSH, FSH, LH, HCG.
- Polypeptide - PTH, Calcitonin, Relaxin, Somatomedin, Oxytocin & ant. pituitary Hm (GH, PRL, Somatostatin, ACTH) ----- mnemonic CASPOR-G.
- Biogenic amines (catechol amines) - Adr, NA, T₄, DA

Second Messenger

- Hormones that bind to cell surface receptors (2nd messenger Ca²⁺ or phosphatidyl inositols or both)
Ach, Angiotensin II, ADH, CCK, Gastrin, oxytocin, PDGF, Substance P, TRH, GnRH
- cGMP as 2nd messenger --- ANF, NO
- cAMP as 2nd messenger --- ACTH, ADH, hCG, FSH, Glucagon, LH, PTH, TSH, E, NE, secretin, lipotropin

- Kinase/ phosphatase cascade as 2nd messenger
Erythropoietin, insulin, growth Hormone, prolactin

M/A of hormones / drugs

Hormones that bind	Acts at / 2 nd messenger	Examples
Intracellular receptor	Cytoplasmic receptors	Steroidal Hm - Gluco - Mineralo - Estrogens - Progestins
	Nuclear receptors	Thyroid hormones ((T ₄ T ₃))
Cell surface/ membrane receptors	by ↑ing cAMP	Glucagon, calcitonin, PTH, TSH, ACTH, Gn (FSH/LH) hypothalamic releasing Hm)
	by ↑ing IP ₃ / DAG or Ca ⁺⁺	Oxytocin, ADH (vasopressin)
	by activation of enzyme tyrosine protein kinase	Insulin, GH

- Intracellular receptors are slowest acting receptors. These may be present in the **cytoplasm** (Gluco, mineralo, VitD) or in the **nucleus** (for thyroid hormones, Retinoic acid, and PPAR, estrogen, progesterone, androgens, testosterone). Both type of receptors finally act by nuclear mechanisms.

Steroid receptor supergene family hormones

These hormones bind intracellular receptors

- Cortisol /Gluco-,mineralo & sex steroid (progestins)
- Vit. D (esp D3 form)
- Retinoic acid
- Thyroid hormone
- V-erb-A

→ Androgen receptor belongs to nuclear receptor superfamily

Drugs acting through nuclear receptors

T₃, T₄, VitaminD, Retinoids, Rosiglitazone, Pioglitazone etc.

Proteomics

Study of protein structure and functions in biological processes like disease.

SOME IMPORTANT NEGATIVE POINTS

- Acetoacetic acid (KB) & fatty acids — are NOT substrate for glucose synthesis

- Sedoheptulose PO_4 — is NOT a product of pentose pathway
- Phosphate — is NOT a component of Ganglioside
- HMG CoA is NOT involved in — Isoleucine metabolism
- NOT a secondary messenger — Guanyl cyclase
- Structure of protein can NOT be determined by — HPLC
- Phosphoenol pyruvate — is NOT produced directly from pyruvate.
- Enzyme NOT used in gluconeogenesis — Pyruvate dehydrogenase
- Hydrogen bond — is NOT present in primary structure
- Covalent bond — is NOT present in antigen - antibody complex or enzyme substrate complex
- Pyridoxal phosphate — is NOT required for hydroxylation of proline in collagen synthesis
- Tyrosine — is NOT an essential aa (but it becomes essential in PKU).
- Glutamate is NOT a precursor of — Histidine
- Reaction which does NOT occur in glycolysis — Hydration
- Rothera's test detects ketone bodies but it can NOT detect — β -hydroxy butyrate
- Biotin is NOT required as a coenzyme in — Pyruvate dehydrogenase (It requires thiamine)
- Sphingomyelin does NOT contain — Lecithin
- Cherry red spot is NOT seen in — Gaucher's d/s
- Hepatomegaly is NOT seen in — Hepatic porphyria
- Ligase chain reaction is NOT useful for — Detection of mutation
- Tissue which can NOT catabolize acetoacetate to CO_2 , H_2O , and usable energy — Brain and liver
- NOT true about lipoprotein lipase — Does not require apo CII as a cofactor
- The concentration of 2,3 BPG in red cells does NOT increase in response to — Hypoxanthine
- In humans acetyl Co A can NOT directly give rise to formation of — Glucose
- Insulin does NOT cause — Ketogenesis
- Free radicals in lens are NOT held by — Vitamin A
- cAMP is NOT a 2nd messenger for — Dopamine
- Amino acid which can NOT be phosphorylated by prokaryotic protein kinases — Asparagine
- NOT true of glutathione — Converts Hb to Met-Hb
- Eukaryotic membrane does NOT contain — Triglycerides
- NOT a cause of fasting hypoglycemia — Glucagon excess
- Does NOT occur when liver glucose is short — Increase in fructose 2,6 biphosphate
- NOT degraded by colonic flora — Lignin
- TPN does NOT provide — Fibre
- NOT true about trace elements — Zinc deficiency causes pulmonary fibrosis
- NOT true about HDL — Can oxidise LDL
- Free radical are NOT produced by --- Glutathione peroxidase
- NOT a method of total protein estimation — Bromocresol green assay (BCG assay).
- NOT true about oxygenase enzyme --- Involved in carboxylation of drugs.
- Enzyme NOT acting in fasting to decrease glycogen --- Angiotensin.

CLINICAL VIGNETTES

- A lady presents with hyperpigmentation of palms & soles with back pain, urine showed green color and black sediment with benedicts test, intervertebral disc calcifications. Most probable diagnosis is: [AIIMS May'10]
- A. Alkaptonuria B. Phenylketonuria
C. tyrosinemia type 2 D. Arginosuccinic aciduria
(Ans. Alkaptonuria)

Alkaptonuria is AR inborn error of metabolism which is caused by deficiency of enzyme *homogentisic oxidase*. Clinically it is c/by arthritis, ochronosis (intervertebral calcification), back pain, renal and prostatic calculi. Urine turns dark/black on exposure to air d/to presence of homogentisic acid. T/t or prevention of severity by Vitamin C.

PKU is also an AR IEM which is caused by deficiency of enzyme *phenylalanine hydroxylase*. Clinically it is c/by mental retardation, seizures, blue eye, hypopigmentation (blue eyed blonde). There is mousy odour of urine and it turns green with $FeCl_3$. TMS (Tandem Mass Spectrometry) is used for prenatal diagnosis.

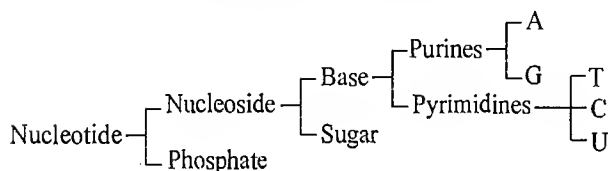
Tyrosinemia type 2 is also an AR IEM which is caused by deficiency of enzyme *tyrosine transaminase*. Clinically it is c/by mental retardation, skin lesions, friable and tufted hairs.

HISTORICAL

- X-linkage was first discovered in *Drosophila* (fruit flies).
- DNA model was given by Watson & Crick.

NUCLEIC ACIDS AND THEIR METABOLISM

- There are two types of nucleic acids DNA and RNA
- DNA is a polymer of nucleotides. The fundamental unit of nucleic acid is nucleotide.
- DNA is found only in cell nuclei but RNA is found both in the nucleus as well as in the cytoplasm.



Purines and Pyrimidines

- The major purines found in nucleotides and nucleic acids are adenine and guanine. Uric acid is the final oxidation product. Intermediate oxidation products are hypoxanthine and xanthine.
- **Purines** – Adenine
– Guanine
– Uracil
- **Pyrimidines** – Thymine
– Cytosine

Adenine ribose = Adenosine

Adenine ribose PO_4 = AMP

Adenosine ribose phosphate-phosphate = ADP

Hypoxanthine ribose = Inosine

- **Bonding (Hydrogen bonds)** In DNA --- A = T, G \equiv C
In RNA --- A = U, G \equiv C
- **Chargaff's rule** : Ratio of purine to pyrimidine bases in the DNA molecule is always 1.

$$\frac{G + A}{T + C} = 1$$

- The 4 nitrogen atoms in purine ring are formed by amino acids - Glycine, glutamine, aspartic acid.

- Uracil is NOT found in DNA and thymine is not found in RNA
- Thermostability of DNA is mostly d/to triple hydrogen bonds b/w G & C. Bond G \equiv C is resistant to melting or denaturation
- Melting of DNA molecule increases the optical absorbance of purines & pyrimidines
- Bromodeoxyuridine is a thymidine analogue
- End product of catabolism of purine nucleotides (A, G) in humans is uric acid and in mammals is allantoin
- Gout is a metabolic d/s of purine catabolism c/by hyperuricemia, attacks of arthritis, deposition of MSU crystals in connective tissues (tophi) and kidneys
- Lesch-Nyhan syndrome is XR disorder a/w complete deficiency of HGPRTase, therefore inability to salvage hypoxanthine or guanine, from which excess uric acid is produced.

DNA

- Human DNA consist of 3 billion base pairs of DNA per haploid genome.
- Each human nucleus contain total DNA length of 2 metre if stretched end to end.
- Consist of double stranded helix with an anti-parallel orientation.
- Two strands are held together by hydrogen bonds. Vanderwals, and hydrophobic interactions are also seen.
- Follows base pair rule and is **semiconservative**
- **B-DNA** ---- Most common DNA
- **Z-DNA** ---- Left handed helix
- **C-DNA** ---- DNA without introns. ssDNA molecule that is complementary to an mRNA molecule.
- **Hyperchromic effect**
Melting of DNA is determined by its base composition (Denaturation at high temperature). Temperature at which DNA is half denatured is K/as T_m of DNA.
- **Annealing**
Once the DNA strands are separated they can be renatured by A~. Occur only below T_m (usually $<70^\circ\text{C}$ and fastest at 50°C).
- **Triplex DNA** is d/to " Hoogsteen pairing". " Hoogsteen pairing" is an alternate base pairing pattern, more commonly seen in RNA.

DNA SYNTHESIS

Chromosomal (DNA) replication

- Occurs during the S phase of cell cycle. In the S-phase DNA and histone are synthesized to form chromatin
- The structure of chromatin affects the timing of replication
 - DNA packaged as heterochromatin is replicated in late S- phase (e.g. inactive X-chromosome or Barr body)
 - The active X chromosome packaged as euchromatin is replicated in early S- phase
- DNA polymerase I (also called Kornberg's enzyme or DNA dependent DNA polymerase) is the major enzyme required for DNA replication
- DNA polymerase require a RNA primer to start DNA synthesis.
- DNA polymerase copy a DNA template in the 3' to 5' direction & new DNA strands are synthesized in 5' to 3' direction
- Replication is semiconservative
- Human DNA has multiple replication origins
- Enzyme DNA helicase recognizes the DNA origin & open the double helix at that site.

Proteins/Enzymes involved in Replication

- DNA primase --- Initiates synthesis of RNA primers.
- DNA topoisomerase --- Relieves torsional strain that results from helicase induced unwinding (removes supercoils of DNA). Strand separation.
- Helicase --- Unwinds the DNA in 5' to 3' direction preceding replication forks in order to provide single-strand template for replication.
- DNA Gyrase --- Introduce negative supercoils into the resting DNA .
- RNA Dependent DNA polymerase --- Enzyme derived from RNA tumour viruses that makes complementary (Reverse transcriptase) DNA (cDNA) copies from RNA templates
- Restriction endonuclease --- Cut the DNA into fragments at specific DNA sequences.
- DNA ligase --- Seals the single strand nicks b/w the nascent chain & Okazaki fragments on lagging strand.

- Okazaki fragments are short stretches of discontinuous DNA on lagging strand, formed during ss DNA replication
- A telomere is a nucleotide sequence at the end of a chromosome. A telomere allows replication of linear DNA to its full length.
- Separation of double stranded DNA into single strands is k/a melting of DNA
- DNA polymerase synthesize --- DNA from DNA
- RNA polymerase synthesize --- RNA from DNA
- Reverse transcriptase synthesize --- DNA from RNA (RNA---DNA---RNA)

Mechanisms of DNA repair

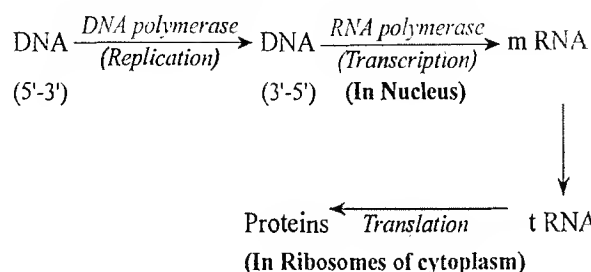
Mechanism	Problem	Ds d/to defect
1. Mismatch repair	Causes errors when DNA is copied	Hereditary non-polyposis colon cancer
2. Base-excision repair	Spontaneous/ chemical/ radiation damage to a single base (depurination of DNA)	
3. Nucleotide excision repair	Used to replace regions of damaged DNA upto 30 bases	Xeroderma pigmentosum
4. Double strand break repair	Involved in Immunoglobulin gene arrangement	

Clinical syndromes a/w increased risk of skin cancers and leukemias are ---

- Ataxia telangiectasia is an AR disorder in which there is increased sensitivity to X-rays and UV rays is seen.
- Bloom's syndrome is c/by chromosomal breaks and rearrangements (d/to defective DNA ligase)
- Fanconi's anemia an AR disorder is a/w chromosomal instability, probably have defective repair of cross-linking damage.
- Xeroderma Pigmentosa is an AR condition in which cells can not repair damaged DNA. Marked sensitivity to sunlight resulting in skin cancers and premature death

PROTEIN SYNTHESIS

Central Dogma of Molecular Biology



Initiation

- In prokaryotes initiation step of protein synthesis require --- f- met t RNA (N-formylmethionyl-t-RNA)
- In Eukaryotes all polypeptides are synthesized by cytosolic ribosomes which begin with methionine
- Capping helps in attachment of mRNA to 40s ribosomes. 5'cap is involved.

Transcription

- Mechanism by which cells copy DNA to RNA
- Occurs in the nucleus
- It is performed by one of the 3 enzymes
RNA polymerase I---which produces rRNA
RNA polymerase II---which produces mRNA
RNA polymerase III---which produces tRNA & 5S rRNA
- RNA polymerase copy a DNA template strand in 3'to 5' direction which produces an RNA transcript in the 5'to 3' direction

Translation

- Mechanism by which the mRNA nucleotide sequence is translated into the aminoacid sequence of a protein
- Occurs in the ribosomes of cytoplasm using RER
- It uses tRNA.
- It uses the enzymes aminoacyl-tRNA synthetase (which links an aminoacid to tRNA.) & peptidyl transferase (which helps to form peptide bond b/w amino acids)
- Ribosome moves along the mRNA in a 5' to 3' direction. The NH₂ terminal end of a protein is synthesized first & COOH end the last.
- Poly (A) tail is translated into polylysine as AAA is the codon for lysine.

Translocase --- Enzyme required for elongation of peptide chain

Peptidyl transferase --- Enzyme required for formation of peptide bonds.

Amino-acyl t-RNA synthetase --- In translation proof reading of mRNA is done by aminoacyl t-RNA synthetase (**Fidelity enzyme**)

Post transcriptional modification of mRNA

- Occurs in nucleoplasm
- Poly A tailing end is 3' end & capping occurs at 5' end
- Splicing of exons of coding part (exons exist) & removal of introns-non coding part

Transcription factors/ Gene regulatory proteins

Control of transcription requires high affinity and specificity in binding regulatory proteins to the correct region of DNA, which is provided by motifs. They bind to DNA through the interaction of a/a & nucleotides

- DNA binding proteins are *Homeodomain protein*, **Zinc finger motif**, helix loop-helix motif, Leucine zipper
- Receptors of glucocorticoids, estrogen, progesterone, thyroid, retinoic acid, vitD3 are examples of Zn finger proteins.

Major classes of RNAs

	mRNA	rRNA	tRNA
<i>In Prokaryotes</i>			
	5% of total	Most abundant (80%)	15% of total RNA
	Polycistronic	-	Extensive intrachain base pairing
<i>In Eukaryotes</i>			
Structure	Monocistronic	Most abundant structural component of ribosomes	Clover leaf 2 ^o structure, Anti-codon arm+
Synthesis	from hnRNA	In nucleolus	Cytoplasm
Feature	Carries information from nucleus to cytoplasm		Abnormal purine & pyrimidine bases TψC, pseudouridine present
			Classifica ^a is based on extra arm (variable)
Role in protein synthesis	Acts as a template for it	Elongation of peptide chain during protein synthesis	Carrier of amino acids, decodes the information in DNA

- Like rRNAs, tRNAs in both bacteria and eukaryotes are synthesized as longer precursor molecules (pre-tRNAs), some of which contain several individual tRNA sequences. In bacteria, some tRNAs are included in the pre-rRNA transcripts.

● *Post transcriptional processing of tRNA the 5' end of pre-tRNAs involves :*

- **5' end capping & Poly A tailing**
- Cleavage at the 5' end of the tRNA is catalyzed by the RNase P ribozyme
- Cleavage at the 3' end is catalyzed by a conventional protein RNase.
- Addition of CCA terminus to the 3' end of many tRNAs in a posttranscriptional processing step.
- Finally, some bases are modified at characteristic positions in the tRNA molecule.

Micro RNA (Mi RNA)

ssRNA molecules which down regulate gene expression.

They are not translated into proteins (non-coding RNAs).

They were found to be a/w **CLL** and **heart diseases**. When Mi RNA binds mRNA ---RISC (RNA Induced Silencing Complex) is formed. This process is k/a *Gene silencing*.

Small RNA

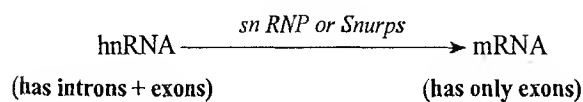
Small RNA are of two types : Sn RNA and SiRNA

Small nuclear RNA (Sn RNA)

- A/w SNURPs proteins.
- It acts as an enzyme (ribozyme) *on phosphodiesterase bond of RNA* and is important in **splicing reaction** (i.e. they convert hn RNA to mRNA).
- Six types are found from U1 to U7 except U3. U1-U6 help in splicing while U7 helps in stem loop structure attachment to histone mRNA.

Splicing reaction

After transcription RNA are modified , the process in which introns (RNA sequences which do not code for proteins) are removed & exons (RNA sequences which code for proteins) are joined (remember EXON EXISTS).



Small interference RNA (Si RNA)

- Role in gene regulation.
- They bind the complementary sequences of functional mRNA and thus inhibit or block their expression.
- Tried as a mode of gene knock out. Role in defending cells against parasitic genes, viruses and transposons.

→ *RNAi path is found in many Eukaryotic cells including animals and is initiated by the enzyme Dicer, which cleaves long dsRNA molecules into short fragments of ~ 20 nucleotides.*

→ *Ribozymes are protein molecules with intrinsic catalytic/enzymatic activity (e.g. Sn RNA & r RNA).*

→ *Aptamers are a special class of are oligonucleic acid (oligonucleotide) or peptide molecules that bind to a specific target molecule . These small RNA/DNA molecules can form secondary and tertiary structures & are capable of specifically binding proteins or other cellular targets; they are essentially a chemical equivalent of antibodies.*

→ *Defective splicing of hn RNA leads to β -thalassemia & spinal m/s atrophy. (hn RNA is found in these d/s)*

● **Exons** --- Are transcribed portion of genes that are retained in processing of hnRNA→mRNA. Term 'Exon' stands for expressed portion of genes (remember **exon exists**).

● **Introns** --- Transcribed portion of genes that are removed (not translated)

● **Cistron** --- Smallest fundamental unit of gene expression which codes for DNA synthesis

● **Operon** --- Is the segment of DNA strand, contain cluster of several genes

→ *Ends of mRNA molecule are involved in mRNA stability. The 5' cap structure in eukaryotic mRNA prevents attack by 5'exonucleases.*

→ *In the Lac Operon, catabolite gene activator protein (CAP) is responsible for positive regulation*

HISTONE

- Helps in condensation of DNA into chromosomes.
- There are 5 classes of histone : H1, H2A, H2B, H3, & H4.
- These small proteins are positively charged at physiological pH as a result of their high content of arginine and lysine.
- Acetylation enhances transcription and promotes euchromatin formation.
- De-acetylation and methylation represses transcription and promotes heterochromatin formation..

CODONS

- Codon is composed of 3 nucleotide bases. i.e. it is a triplet code.

- 61 codons code for amino acids .
- **Initiating codon** is ---AUG which codes for methionine in eukaryotes & GUG in prokaryotes.
- 3 codons do not code for any a/a . These are UAA(Ochre), UAG (Amber), UGA (Opal) hence they are termed as termination codon / stop codons or **non sense codons**. It indicates that synthesis of protein coded by mRNA is completed.
- The genetic code is degenerate becoz there are many instances in which different codons specify the same amino acid. i.e. more than one codon codes for same a/a . Degeneration of codons is at the level of translation.

CHROMOSOMAL ANALYSIS

Cytogenetic Techniques

Karyotyping

Sample of cells are fixed and stained to create light and dark bands and the picture of chromosome is analyzed. Typically used to detect **germline** aneuploidies.

FISH

Fluorescence in situ hybridization is used to detect and localize the presence of **specific DNA sequences** on chromosomes. Used for species identification, genetic counselling

Micro-array

Chromosomal Microarray Analysis (CMA) is a molecular cytogenetic method for analysis of copy number changes in **DNA content** of specific subject.

cGH Array (Comparative Genomic hybridization)

CGH detects only **unbalanced** chromosomal changes. Structural chromosomal aberrations e.g. balanced translocations or inversions can **not** be detected by CGH or CMA.

- **MAPH** : Multiplex Amplification & Probe Hybridisation.
- **MLPA**: Multiplex Ligation Dependant Probe Amplificaⁿ.
- **MALDI** : Matrix Assisted Laser Desorption & Ionisation
- **FRAP** :

Fluorescence Recovery After Photobleaching. Movement of protein from nucleus to cytoplasm is seen.. Used to assess the structure of membranes (Fluid mosaic model in the past).

Analysis of nucleic acids

- *Northern blot* is used for — **RNA analysis**
- *Southern blot* is used for — **DNA analysis**
- *Western blot / immunoblot* is used for — **Protein analysis**.
- *Gene knock out* is used to demonstrate — **Gene expression & function of gene analysis**

Techniques for Detection of Mutation

- Agarose gel electrophoresis--Basic technique used for separation of DNA is electrophoresis.
- SSCP (Single stranded confirmational polymorphism)
- Dideoxy nucleotide tail sequencing : developed by Fredrich Sanger in 1977.

PRENATAL DIAGNOSIS

Sample of cells obtained by amniocentesis or CVS is used for prenatal diagnosis. Pregnant women of 35 or + are candidate for prenatal diagnosis as risk of aneuploidy is higher in woman of age 35 or more.

Prenatal Diagnosis for genetic disorders

Several single gene disorders are diagnosed prenatally by DNA analysis

- **AD disorders:**
 - Huntington's ds
 - Myotonic dystrophy
 - Neurofibromatosis
- **AR disorders:**
 - Sickle cell anemia
 - Cystic fibrosis
 - Thalassemia α & β
 - Tay-sachs d/s
 - PKU (Phenylketonuria)
- **X-linked disorders:**
 - Hemophilia A&B
 - Duchenne type m/s dystrophy

- Prenatal d/g of neural tube defects is not possible by Chorionic villous sampling
- Muscle dystrophy can not be diagnosed by CVS or amniocentesis. Muscle biopsy is diagnostic.
- Prenatal d/g of hemophilia is based on linkage analysis. Genetic linkage analysis c/b performed by RFLP
- Microarray technique is used for detection of differences in gene expression (in pathogenesis of malignancy)

DNA fingerprinting

- Done by nucleated cells e.g.
Blood - WBCs, RBCs, BM,
Semen, vaginal epithelial cells
Tooth pulp, hair root, m/s, skin, mucous membrane
- Uses RFLP or repeat sequence DNA to establish pattern of DNA for individual.

Genetic basis of diseases

- Around 50% of abortions, 50% of congenital anomalies, 50% of mental retardation, 50% of deafness, 50% of blindness and 15% of cancers have genetic basis

XR

- Manifests only in males. E.g. hemophilia which manifests only in boys
- All females are carrier (do not manifest the disease)
- Son of female carrier, 50% are affected
Daughter of female carrier, 50% are carrier

XD

- No male to male transmission
- Only females affected

AD

- Vertical inheritance
- 50% chance of inheriting a d/s
- Variable expressivity/ incomplete penetrance is seen in AD disorders.
- AD disorders are manifested in the heterozygous state, so at least one parent of an index case is usually affected.
- When an affected person marries an unaffected person -- Every 1 child of 2 has chance of having d/s (50%)
- If both parents have d/s (heterozygotes) --- Chances of having an unaffected baby are 25%
- If both parents are homozygotes --- all the children will be affected [0% children will be unaffected]

AR

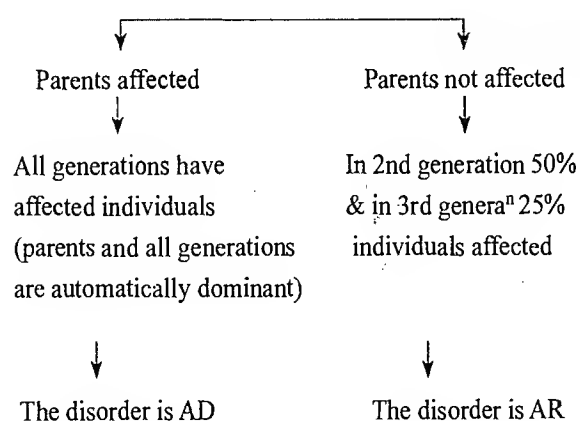
- Horizontal inheritance. Transmitted in many siblings.
- 25% chance of affecting a child
- 50% are carrier
- Complete penetrance is seen

How to approach inheritance pattern through pedigree chart

- First of all in a generation look for..if only one sex is affected...
Condition a: only males affected
(*Mama - Bhanja effect*) only males with maternal uncles affected → The disorder is X LINKED RECESSIVE. E.g. hemophilia which manifests only in boys.

- Condition b: only females affected
(*Baap - beti ka pyar*) affected males transmit only to their daughters → The disorder is X LINKED DOMINANT

- If there is no sex bias → look for affected parents



- In some AD disorders (e.g. Osteogenesis imperfecta) phenotypically normal parents have >1 affected child. This is exception to normal Mendelian inheritance. This is d/o germline or gonadal mosaicism.
- In AD disorders some individual inherit the mutant gene but phenotypically normal. This is d/o incomplete penetrance. 50% penetrance means 50% individual who carry the gene express the trait.
- If trait is seen in all individuals carrying the mutant gene but expressed differently among individuals, it is called variable expressivity. Seen in neurofibromatosis type I.

TRINUCLEOTIDE (TRIPLET) REPEAT DISEASES

Expansions affecting	Repeat sequence	Ds	Inheritance	Affected protein
CODING regions	CAG	HD	AD	Huntington
	CAG/CTG	Spinocerebellar ataxia	AD	Ataxin (α_{1A} of Ca-channel) in type 6
		Spinobulbar atrophy	XR	Androgen receptor
NON-CODING REGIONS	CGG	Fragile-X syndrome	XD	FMR-1
	CTG	Myotonic dystrophy	AD	DM protein kinase
	GAA	Friedreich's ataxia	AR	Frataxin

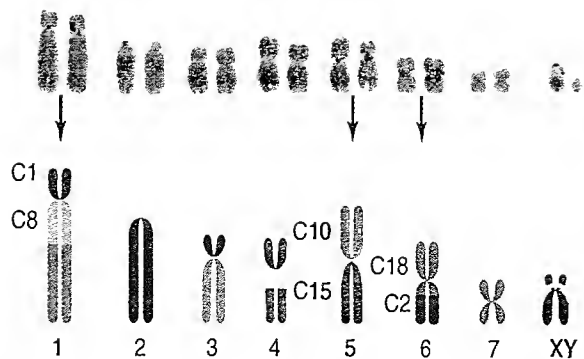
- More is the number of repeats, more is the mental retardation.
- Anticipation phenomena is present in triplet repeat diseases i.e. with each generation severity of d/s becomes more.

CHROMOSOMES

Chromosome groups

Group	Type	Chromosome number
A	Large metacentric	1,2,3
B	Large or very submetacentric	4,5, XX
C	Mid submetacentric	6,12,
D	Mid acrocentric	13, 14,15 Satellite chromosomes
E	Sub metacentric	16,17,18
F	Metacentric	19,20
G	Acrocentric	21,22,Y Satellite chromosomes

- Smallest human chromosome is chromosome 22.
- Chromosome 22 is the first human chromosome to be sequenced in its entirety in 1999.



CHROMOSOMAL ASSOCIATIONS

Chr. No.	A/w
1	Rh blood groups, neuroblastoma, NPHS-2 (1q25-31)
2	Cystinuria, abetalipoproteinemia
3	RCC, VHL syndrome, alkaptonuria
4	Huntington's chorea
5	FAP/ colon cancer (5q), Cri-du-cat (5)
6	HLA/Major or minor HC antigen system (6p), DM, hemochromatosis (HFE gene)
7	Cystic fibrosis
8	Osteopetrosis
9	Inheritance of ABO blood groups (9p), Friedrich's ataxia
11	Gene for β -globin chain (SCD, Wilm's (11p13), MEN I, Ataxia telangiectasia, human insulin gene, PTH hormone)
12	PKU, vWF
13	Retinoblastoma (13q14), osteosarcoma, Wilson's (ATP7B gene) d/s, BRCA-2
14	α -1 anti-trypsin deficiency, Familial HOCM
15	Marfan's, Prader Willi, Angelman's, albinism, Fanconi syndrome
16	α thalassemia
17	Breast carcinoma (BRCA-1), ovarian carcinoma, neurofibromatosis(NF-1), medulloblastoma (17p)
19	Myotonic dystrophy, insulin receptor, NPHS-1 (19q13)
20	DM type I (MOD)
21	Homocystinuria, amyloidosis
22	Meningioma, acoustic neuroma, neurofibromatosis(NF-2), Di George syndrome
Xq	Gene for androgen receptor, Testicular feminization (androgen insensitivity synd), Fragile -X syndrome (Xq27)

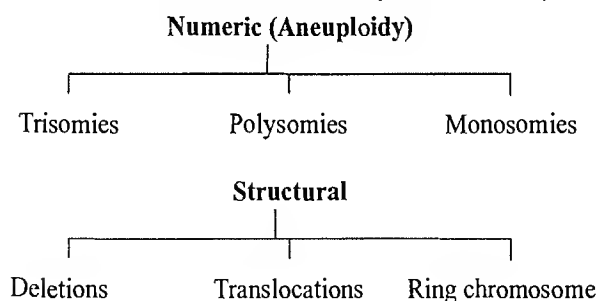
- **Chromatin** --- Consist of double helical DNA + histones + nonhistone proteins
Euchromatin is the region of DNA that is dispersed (relatively uncondensed) & transcriptionally active
- **Nucleosome** --- Is the basic unit of chromatin packaging and consist of DNA coiled around histones.
- X chromosome is bigger than Y chromosome.
→ *Microsatellite sequence is short sequence (2-5) repeat DNA*

Chromosomal Disorders

- Autosomes are categorized into 7 subgroups A-G. Smallest autosome is 22. Among sex chromosomes Y is smaller than X.
- Karyotype map is made on the basis of size. In Denver's size system X-chr. comes b/w autosomes 6 & 7.
- Chromosomal studies can be conducted on lymphocytes, bone marrow cells, fibroblasts, amniotic fluid cells, chorionic villous cells and fetal blood (but NOT on monocytes).
- In DNA analysis which is NOT used - skin sample.
- **Karyotyping** is used for chromosomal abnormalities. In this cells are cultured and cell division is arrested in **prophase/metaphase** and then stained. Trypsin-Giemsa stain-is used for studying **G** bands, while **Quinacrine** stains for **Q** bands.

→ *Fluorescent DNA probes are used to identify homologous DNA segments using FISH.*
→ *Feulgen reaction is used to detect DNA*
→ *Chromatin (chromosomal material) contains — ds DNA, basic protein histone, some non-histone proteins, RNA*

Chromosomal Abnormalities (Aberrations)



- *Incidence of chromosomal anomalies is 0.4% in live births.*
- *Trisomies are m/c numeric abnormalities while deletions are m/c structural abnormalities.*
- *Common trisomies are — 21 (commonest), 18 and 13*

Aneuploidies

- Aneuploidy is abnormal number (> 46 or < 46) of chromosomes which results from non-disjunction in meiotic division --- the failure of a chromatid pair to separate in a dividing cell.

It may be ---monosomy (X in place of XX, A in AA), disomy, trisomy or polysomy

Clinical phenotypes ---

Trisomy 13	47, XX or XX, + 13	Patau
Trisomy 18	47, XX or XY, + 18	Edward
Trisomy 21	47, XX or XY, + 21	Down's
Klinefelter's	47, XXY	
Turner's	45, X	
Superfemale	47, XXX	

- Methods used for detection of aneuploidies --- FISH, Micro array, Spectral karyotyping

Deletions :

Among structural abnormalities deletions are most common. Deletions are a/w mental retardation and congenital malformations. Deletions in long arm of chromosome are designated q^- and that in the short arm as p^- . e.g.

- 5 p^- Cri-du-chat (cat cry) syndrome
- 11 p^- Wilms tumour
- 13 q^- Retinoblastoma

- **Micro-deletions** are small deletions that may be visible only in high quality prophage preparations. e.g. Duchene MD, William's and Di George syndromes.

- **Ring chromosome** is d/to deletion of each end of chromosome and joining of the sticky ends.

EXCEPTION TO SIMPLE MENDELIAN INHERITANCE

Mitochondrial inheritance

"All mitochondria are contributed by the ovum during zygotic formation — it is transmitted by maternal non-mendelian inheritance". Inherited mitochondrial disorders are transmitted in a matri-lineal fashion. All children from an affected mother (Mutations in mtDNA) will inherit the d/s, but it will not be transmitted from an affected father to his children.

- Human mitochondrial DNA (mt DNA) is a double stranded circular molecule containing 16,569 base pairs.
- Examples of selected mitochondrial diseases
 - Leber's hereditary optic atrophy
 - Kearns Sayre syndrome
 - MELAS
 - Chronic progressive external ophthalmoplegia
 - Pearson's syndrome
 - MERRF syndrome

Mosaicism

Presence of ≥ 2 distinct cell lines in the tissue of an individual.

- Chromosomal mosaicism from non-disjunction results in Turner's syndrome.
- Somatic mosaicism d/to mutations (*non-disjunction occurs in mitosis*) E.g. in $G_s\alpha$ results in the McCune-Albright syndrome.

Genomic Imprinting (GI)

Imprinting refers to selective inactivation of a gene or a set of genes on either paternal chromosome or on maternal chromosome (autosome). It leads to preferential expression of functional allele of one of the parent. 70- 80% of Prader Willi and Angelman's are d/to genomic imprinting and only 20% are d/to u/L parental disomy (UPD).

Features	Prader-Willi	Angelman's
Chromosome involved	15q 11-13 deletion	15
Mostly d/to	Paternal genomic imprinting (70%)	Maternal genomic imprinting (80%)
Less common cause	UPD (25%) of 2 maternal chromosomes	UPD (2-3%) of 2 paternal chromosomes
Cl/f	↓ Fetal activity neonatal hypotonia, obesity, mental retardation, small hand/feet, Hypogonadism	(Happy puppets) Normal at birth, mental retardation, seizures, ataxia, hypotonia

[Mnemonic to remember : PaPa -G and Uni-MaP means in Prader Willi Genomic imprinting (deletion) of Paternal chromosome is common, while UPD of Maternal chromosome is seen in Prader Willi]

- Other examples of genomic imprinting are ---H.mole, ovarian teratoma, Russel Silver syndrome, Beckwith Wiedmann syndrome (d/to expression of imprinted gene IGF-II)

Uniparental disomy (UPD)

- When both the homologous chromosomes are inherited from single parent and this is k/as "Uniparental disomy" (UPD).
- Expression of AR disorders is seen e.g. cystic fibrosis, sickle cell anemia. D/to meiotic non-dysjunction.
- Maternal UPD occurs in Prader Willi and Paternal UPD occurs in Angelman.

MENDELIAN DISORDERS [single gene disorders]

AD	AR
<ul style="list-style-type: none"> Achondroplasia Acute intermittent porphyria Adult PCKD BRCA1/2 breast cancer MODY (Maturity onset diabetes of youngs) Familial - <ul style="list-style-type: none"> Hypercholesterolemia Hypertrophic CMP Hypercholesterolemia Colonic polyposis Hereditary - <ul style="list-style-type: none"> HNPCC Hemorrhagic telengicatasia Spherocytosis (HS) Huntington's Chorea Hyperlipoproteinemia 1,2,3,4 Von willebrand disease Marfan's syndrome Myotonic dystrophy M/s dystrophy, limb girdle -1 Neurofibromatosis Otospongiosis /otosclerosis Osteogenesis imperfecta Peutz Zeghers syndrome Polydactyly Retinoblastoma vWD 	<ul style="list-style-type: none"> Most IEMs (inborn errors of metabolism) Albinism Alkaptonuria Agammaglobulinemia (swiss type) Ataxia telengectasia α_1 Anti-trypsin deficiency Beta thalassemia Cystic fibrosis Congenital erythropoietic porphyria (CEP) CAH, 21-Hydroxylase def. Fredrich's ataxia Fanconi's syndrome Glycogenosis, Gaucher's ds., PK deficiency Hirschsprung's disease Lysosomal storage ds M/s dystrophy, limb girdle -2 Maple Syrup Urine ds PKU Sickle cell anemia Hemochromatosis Wilson's ds

X-Linked R	X-Linked Dominant
<ul style="list-style-type: none"> • Agammaglobulinemia (Bruton's) • Adult PCKD – colour blindness • Color blindness • CGD (Chronic granulomatous d/s) • Duchenne's and Becker's MD • DI • G-6-P D def. (incompletely dominant expression) • Hemophilia A & B • Ocular albinism • Ornithine transcarbamylase deficiency • Retinitis pigmentosa • Fragile X syndrome 	<ul style="list-style-type: none"> • Alport syndrome • blood group Xg • Fabry's Ds • Familial hypophosphatemia (VDDR, Vitamin D resistant rickets) • Type 3 VDDR, HPDR • G-6-P D def. (incompletely dominant expression) • Incontinentia Pigmenti

Polygenic (multifocal) Inheritance is seen in

- DM
- Essential hypertension
- Cleft lip/palate
- Autism
- Cancers

→ Autosomal Codominance (codominant Inheritance) is seen in — HLA, Blood group Ag.

→ Remember most of the inborn errors of metabolism are AR disorders except — Fabry's ds, G6PD def. (XR), Bruton's agammaglobulinemia, ocular albinism (XR).

→ Disorders with prefix 'hereditary' or 'Familial' are usually AD disorder e.g. FPC (familial polyposis coli, Familial hypercholesterolemia, Hereditary spherocytosis)

Epigenetic effect

- Meiotically and mitotically heritable changes in gene expression not a/w DNA sequence alterations are referred to as epigenetic effects.
- Role in cancer, mental retardation & hematologic disorders and ?aging.

Atavism

- When a child resembles its grandparents it is k/as atavism.
- Best example of atavism is caudal appendages as coccygeal projection.

X-inactivation (Barr bodies)

- Inactive X-chromosome is seen as Barr body /sex chromatin in buccal mucosa & epidermis and as Drum stick in neutrophils. Barr body is found in interphase of cell cycle
- Number of bar bodies = no. of X – 1 (e.g. in Klienfelter it is 1 & in super female xxx it is 2)

Chromosomal Breakage Syndromes

Most are inherited as recessively or may be induced by sunlight, LSD abuse in pregnancy. Examples are

- Fanconi's anemia
- Bloom's syndrome
- Incognita pigmenti
- Ataxia telangiectasia (Louis Bar syndrome) chromosomal breaks + non random rearrangements are seen.

BACTERIAL GENETICS

- *Episome* is an accessory extrachromosomal replicating genetic element that can exist either autonomously or integrated in a chromosome.
- *A plasmid* is a small, circular, ds DNA molecule, which is distinct from chromosomal DNA. It is physically separate from, and can replicate independently of, chromosomal DNA within a cell.

Transduction

Transfer of a portion of the chromosomal DNA /episomes /sometimes plasmids from one bacterium to another by a bacteriophage is k/ as transduction. Used as a method of genetic engineering in the t/t of some IEMs.

Transformation

Transfer of genetic information through agency of free DNA. Studied in pneumococci (Griffith), bacillus species & H. influenzae.

Lysogenic Conversion

The phage DNA becomes integrated with the bacterial chromosome as the prophage, which multiplies synchronously with the host DNA and is transferred to the daughter cells. This process by which the prophage DNA confers genetic information to bacterium is called as lysogenic or phage conversion. In diphtheria it confers toxigenicity.

Conjugation

Process by where by a 'male' or 'donor' bacterium 'mates' or makes physical contact with a 'female' or 'recipient' bacterium and transfers genetic elements into it. *First demonstrated in E Coli K12 strain by Lederberg and Tatum.* The plasmid responsible for conjugation is termed '**sex factor**' or '**Fertility (F) factor**'. F factor is actually an episome.

Methods of gene delivery

- **Transfection** is the process of deliberately introducing nucleic acids into cells.
- There are many methods of introducing foreign DNA (gene) into a eukaryotic cell :
 - Electroporation
 - Magnetofection
 - Sonoporation
 - Gene gun
 - Dendrimers etc.
 - Site directed recombination

- *Transferable drug resistance is seen in Enterobacteriaceae, vibrio, pseudomonas, pasteurilla.*
- *Transposons are called jumping gene.*
- *Plasmids are circular DNA molecules present in the cytoplasm of bacteria, capable of autonomous replication.*
- *Bacteriophage are viruses that parasitize bacteria and consist of a nucleic acid core and a protein coat.*
- *The plasmids determining penicillin resistance in staphylococci is mediated by transduction.*
- *Largest fragment of DNA can be cloned in --- cosmid*

Lactose Operon /Lac Operon

"Lac operon is cluster of genes encoding for proteins involved in lactose metabolism in prokaryotes."

- Operons and polycistronic mRNAs are common in bacteria but differ in eukaryotes.
- Genes in Lac operon:
 - Lac Z : codes for β galactosidase
 - Lac Y : codes for permease
 - Lac A : codes for thiogalactoside transacetylase
- Regulatory portion in Lac operon:
 - Positive regulator : CAP protein & cAMP
 - Negative regulator : Repressor protein
 - Promotor (P) region : Where RNA pol binds
 - Operator(O) region : Where repressor protein binds.

RECOMBINANT DNA TECHNOLOGY

Recombinant DNA Technology

- Joining of 2 different DNA via enzyme ligase is k/a recombinant DNA technology. cDNA is used to insert in to the vector DNA for recombinant DNA technology.
- To produce insulin in bacteria for therapeutic purpose, initial material is mRNA from beta pancreatic cells of human.
- cDNA is the double stranded copy of the cellular mRNA.
- Chromosomal walking involves repeated cloning of overlapping DNA segments. The procedure is lengthy usually cover only 100-200 kilo bases.
- In patient with DNA mismatch repair deficiency mutations accumulate in microsatellite repeats, k/as **microsatellite instability**.

PCR Vs. RFLP

PCR	RFLP
<ul style="list-style-type: none"> • Rapid automated method for amplification of specific DNA sequences. • Process, <ul style="list-style-type: none"> Sample DNA ↓ (denaturation) ssDNA ↓ (Annealing) Primer (ds DNA) ↓ (extension) Multiple dsDNA • Heat stable polymerase (Taq-I) used • Temp. range 50-95°C. • Mutant & Wild type oligonucleotides can be used as a probe to analyze PCR products conversely products of PCR can be used to analyze cDNA libraries. 	<ul style="list-style-type: none"> • DNA is cleaved into fragments using restriction enzyme. • Length of the restriction fragments is altered if the genetic variant alters the DNA • Used to :- <ul style="list-style-type: none"> - Detect human genetic defects (useful in prenatal diagnosis) - Trace chromosome from parent to offspring - Linkage of polymorphism with gene mutation - Direct detection of d/s causing mutations.

- *Vector used to increase the yield of protein produced in recombinant protein synthesis ---Inducible promoter region.*
- *IPTG is a compound added to cells to activate a promoter gene.*

GENE THERAPY

For genetic Diseases

- ADA- SCID
- Chronic Granulomatus Disorder (CGD)

- Hemophilia
- Under trial for congenital blindness, lysosomal storage disease and muscular dystrophy.

For Acquired Diseases

- Cancers : Ad.p53 for head and neck cancer, prostatic cancer, pancreatic cancer
- Neurodegenerative diseases such as Parkinson's Disease and Huntington's Disease
- Viral infections (e.g. influenza, HIV, hepatitis), heart disease and diabetes

CELL DIVISION

Cell division is of 2 types

1. Mitosis – prophase, metaphase, anaphase, telophase
2. Meiosis – consist of 2 successive division.
 - 1st meiotic division
 - 2nd meiotic division – similar to mitosis there is interphase between 1st and 2nd meiotic division.

Steps in 1st meiotic division

Prophase → Metaphase → Anaphase → Telophase



pairing of chromosomes (bivalent)

Prophase :

Leptotene : Chromosomes become visible

Zygotene : pairing of chromosomes (Synapsis/ conjugation) and formation of bivalent

Pachytene : tetrad formation, *crossing-over* and *chiasmata* formation

Diploene : Chromosomes break at the point of crossing with *exchange of genetic material*

Metaphase :

Spindle formation occurs in prometaphase, chromosomes are attached by centromeres and firmly bound (align).

Anaphase :

Chromosomes move from equator to the poles of the cells (centromere does not divide in meiosis)

Telophase :

Chromosomes completely moved to opposite poles.
Chromosomes in each cell reduced to half.

- Chromosomes tend to condense, shorten & thicken in **prophase**. Only at prometaphase chromatids become distinguishable.

Phase	Events	Chromosomal changes
G ₂	Centromere, sister chromatids distinguished	
Prophase	Spindle fibres appear	Condense
Prometaphase	Spindle fibres attach to chromosomes	Condense
Metaphase		Align
Anaphase	Sister chromatids move to opposite pole	Divide
Telophase	Nuclear membrane reforms, Spindle fibres disappear	Decondense
Cytokinesis	Cytoplasm divides	

POPULATION GENETICS

The Hardy-Weinberg Law

- The Hardy-Weinberg principle states that allele and genotype frequencies in a population will remain constant from generation to generation in the absence of other evolutionary influences. These influences include non-random mating, mutation, selection, genetic drift, gene flow and meiotic drive.

- Punnett square for Hardy-Weinberg :

		Females	
		A(p)	B(q)
Males	A(p)	A(p)	AB(pq)
	B(q)	AB(qp)	BB(q ²)

- Punnett square for Hardy-Weinberg : The sum of the entries is $p^2 + 2pq + q^2 = 1$, as the genotype frequencies for an infinite population size) must sum to one.

OTHER IMPORTANT POINTS

- *Single nucleotide polymorphism (SNP)* transgenomic Wave Denaturing High Performance Liquid Chromatography (Wave /DHPLC) is an approach that can detect single base pair differences b/w otherwise identical 750 bp fragments of DNA.
- BLAST (Basic Local Alignment Search Tool) is used to compare short sequences of proteins & nucleic acids.
- Oligomismorm gene used in primer --- Error based PCR

- Luciferases are oxidative enzymes used in bioluminescence in genetic engineering.

→ *Entrez Gene & Hap Map are used to identify single nucleotide polymorphism that may contribute to pathological conditions*

→ *CDART, MMDB, and VAST are used to analyze the domain structure & 3-d structure of proteins*

SOME IMP. NEGATIVE POINTS

- Technique which is NOT used to introduce genome into bacteria--- FISH.
- NOT a method of introducing gene in target cell --- FISH.
- Technique which is NOT used to diagnose subtelomeric rearrangements of genes --- MALDI
- Chromosomal studies can NOT be performed on --- Monocytes.
- Mitochondrial DNA do NOT contain --- Introns.
- Do NOT require in PCR --- Dideoxyribonucleotides..
- Material which is NOT involved in protein translational in eukaryotes --- RNA polymerase.
- NOT true for cytosolic mRNA --- Obtained from nuclear DNA.
- Chromosomal mutations can NOT be identified from--- Denaturing gradient gel electrophoresis.

CLINICAL VIGNETTES

- A couple with a family history of beta thalassemia major in distant relative, has come for counselling. The husband has HbA2 of 4.8% and his wife's HbA2 was 2.3%. The risk of having a child with β thalassemia major is:

[AIPGMEE 2003, DNB HRH Delhi 2008]

- A. 50% B. 25%
 - C. 5% D. 0%
- (Ans.: 0%)

- An albino girl gets married to a normal man. What are the chances of their having an affected child and what are the chances of their children being carriers?

[AIPGMEE 2003, DNB HRH Delhi 2008]

- A. None affected, all normal
- B. All normal

C. 50% carriers

D. 50% affected, %50% carrier

(Ans.: None affected, all carriers)

- The mother has sickle cell disease; father is normal; Chances of children having sickle cell d/s and sickle cell trait respectively are:

[AIPGMEE 2001, DNB HRH Delhi 2008]

- A. 0% and 100% B. 25% and 25%
- C. 50% and 50% D. 10% and 50%

(Ans.: 0% and 100%)

SCD is an AR disorder. In an AR disorder diseased is represented by alleles A^+A^+ A normal individual is represented as A^-A^- and carrier is represented by alleles A^-A^+ . So possible outcomes in this case would be :

	A^+	A^+
A^-	A^-A^+	A^-A^+
A^-	A^-A^+	A^-A^+

100% offsprings are carrier (A^-A^+) and none is affected

- Kamlesh 2 year old girl has Down syndrome. Her Karyotype is 21/21 translocation. What is the risk of recurrence in subsequent pregnancies if the father is a balanced translocation carrier

[AIPGMEE 2003, DNB HRH Delhi 2008]

- A. 0% B. 25%
- C. 50% D. 100%

(Ans.: 100%)

- 32 year old female concerns over her baldness. There is history of baldness in her grandfather and maternal grandfather. Risk is due to: [N- review]

- A. AD B. AR
- C. XD D. XR

(Ans.: AD)

Research suggests that the gene for the androgen receptor, which is significant in determining probability for hair loss, (Baldness of the androgenic type) is located on the X chromosome and so is always inherited from the mother's side for men. There is a 50% chance that a person shares the same X chromosome as his maternal grandfather. Because women have two X chromosomes, they will have two copies of the androgen receptor gene while men only have one.

GENERAL PATHOLOGY

Various "Bodies"

- o Asteroid bodies --- Sporotrichosis, Sarcoidosis
- o Civatte (colloid) body --- Lichen planus
- o Councilman body --- Yellow fever
- o Halberstaedter --- Trachoma
- Prowazek's (HP) bodies
- o Leishman Donovan (LD)bodies --- Kala azar (Leishmaniasis)
- o Leventhal- Cole Lillie (LCL)bodies --- Psittacosis
- o Lewy body --- Parkinson's disease
- o Negri body --- Rabies (intracytoplasmic)
- o Miyagawa's granular corpuscles --- LGV(Lymphogranuloma venereum)
- o Psammoma bodies --- Papillary carcinoma of thyroid
(Calcospherites) Serosus cyst adenocarcinoma ovary
Meningioma, mesothelioma
Adenocarcinoma of kidney (RCC), endometrium
- o Russell bodies --- Multiple myeloma
(cytoplasmic inclusions)
Dutcher bodies
(nuclear inclusions)
- o Schaumann's bodies --- Sarcoidosis
- o Verocay bodies --- Neurilemmoma
- o Hirano bodies --- Alzheimer's d/s (seen in hippocampal pyramidal cells)
- o Weibel-Palade bodies --- EM finding in tumours of vascular origin.
- o Henderson-Peterson body --- Molluscum contagiosum
- o Virchow Hassall's body --- Thymus
- o Michaelis Gutmann body --- Malakoplakia of urinary bladder
- o Creola bodies --- Asthma (ciliated columnar epithelial slough)
- o Masson bodies --- Cellular tissue that fills the pulmonary alveoli /ducts in rheumatic pneumonia (modified Aschoff bodies).
- o Sand bodies --- The mass of gritty matter

lying in or near the pineal body, the choroid plexus, and other parts of the brain.

- o Pacchionian bodies --- Arachnoidal granulations.
- o Fergunous bodies --- Masses of mineral matter in the lungs resulting from deposition of calcium /iron salts, and protein around a central core of foreign matter. E.g. in asbestosis

→ Neill-Mooser bodies are seen in Murine typhus d/to *R. typhi*.

→ Rushton bodies are hyaline bodies found in radicular odontogenic cyst.

SOME IMPORTANT CELLS

- o Hurthle cells --- Follicular adenoma of thyroid, Hashimoto's thyroiditis
- o Virchow's cell --- Leprosy (lepra cells). Giemsa-AFB positive cells
- o LE cell --- Is usually a neutrophil seen in SLE, Phagocytic in function
- o Tart cell --- A lymphocyte seen in SLE
- o Langerhans cells --- Antigen presenting cells present in epidermis (modified macrophages)
- o Langhans cell --- Type of giant cell seen in epithelioid granuloma (eg. in TB)
- o Merkel cell --- Present in lower layer of epidermis
- o Muller's cells --- Neuroglia present in retinal epithelium
- o Glitter cell --- Leucocyte with visible movement of cytoplasmic processes, Pathognomonic of pyelonephritis
- o Gitter cell --- Modified microglia in CNS form complex granular corpuscles k/as gitter cells/Hortega cells
- o Flame/Mott cells --- Plasma cell containing glycoprotein globules seen in multiple myeloma

- Foam cells --- Lipid containing macrophages seen in - Leprosy, Xanthomas, Atheromatous plaques, Alport syndrome, and storage diseases (e.g. Niemann Pick ds)
- Clear cell --- Seen in adenocarcinomas (e.g. - RCC)
- Aschoff's cell --- Neutrophil seen in RHD
- Ito cells --- Present in "space of Disse" of liver. Store fats, Vitamin A. Secrete collagenous matrix, provides growth factor. Causes cirrhosis of liver by secreting collagen
- Stave cells --- Spleen
- Tadpole cells --- Seen in pap smear of SqCC of Cx
- Hofbauer cell --- Modified macrophages in chorionic villi of placenta (numerous in early pregnancy)
- Armani Ebstein cells --- Epithelial cells of PCT in patients with diabetes (filled with glycogen vacuoles)

IMPORTANT STAININGS

Substance/ demonstration of	Staining options
◦ RNA	Methyl green pyronin is preferred, (Gallocyanin, acridine orange also c/b used)
◦ DNA	Feulgen reaction, (Gallocyanin, methyl green pyronin also c/b used)
◦ Insulin	Gomori's aldehyde fuchsin
◦ Lipid/fat	Oil red O
◦ Collagen	Von Gieson's/Masson's trichome
◦ Acidic mucin	Best's carmine
◦ Amniotic fluid cells	Nile blue sulphate
◦ Alveolar macrophage	Oil red O, PAS
◦ Bone	Von Kossa
◦ Melanin, argentaffin cells	Masson fontana
◦ Copper	Rubeanic acid
◦ Iron, hemosiderin	Prussian blue

Microorganisms

- Most bacteria --- Gram's stain
- Pneumocystis carinii --- Methenamine silver
- Cryptococcus --- Mucicarmine, Indian Ink
- Plasmodia (Malaria) --- Giemsa (preferred) others - Wright's, field's or Leishman's
- Campylobacter, leishmania --- Giemsa
- H. Pylori --- Warthin starry, Giemsa, silver stain
- Legionella, fungi --- Silver stain
- Mycoplasma --- Diene's
- Inclusion bodies --- Wright's stain

RESPIRATORY BURST

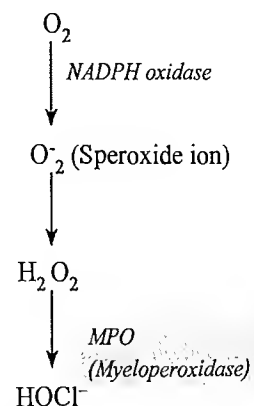
- When neutrophils and other phagocytic cells engulf bacteria, they exhibit a rapid increase in O_2 consumption k/as respiratory burst.
- Respiratory burst involves the activation of oxidases (NADPH- oxidase). It helps in killing of bacteria by bactericidal action.

→ The H_2O_2 MPO (myeloperoxidase) halide system is the most efficient bactericidal system in neutrophils.

→ The binding of opsonized particles to leucocyte Fc or C3 receptors promote phagocytosis of the particles and activates the cells.

Bacterial killing

- There are 2 types of killing of bacteria
 1. O_2 dependent methods : main method
 2. O_2 independent methods
- O_2 dependent method: Oxidative/ respiratory burst



Causes halogenation and lipid peroxidation of bacterial cell wall

- Reactive O_2 species (like $HOCl^-$) have most efficient bactericidal activity.
- $HOCl^-$ causes → halogenation & lipid peroxidation of bacterial cell wall → bacterial killing
- Lactoferrin, lysozyme, BPI, defensins, MBP, elastase and basic cationic proteins are oxygen independent bactericidal mechanisms in phagocytosis
- After internalization of the microorganisms, NADPH oxidase, located in the leucocyte cell membrane, converts molecular oxygen into superoxide ion. Deficiency of NADPH oxidase results in CGD, an X-linked recessive disorder. NBT test is used for diagnosis.
- Catalase is found in nearly all living organisms exposed to oxygen. It catalyzes the decomposition of hydrogen peroxide (H_2O_2) to water and oxygen.
- Glutathione peroxidase protect the organism from oxidative damage. It reduces lipid hydroperoxides to their corresponding alcohols and reduces free hydrogen peroxide to water.

NEUTROPHILIC GRANULES

- *Primary (azurophilic) granules* :
Found in young cells. Contain cationic proteins & defensins that are used to kill bacteria, proteolytic enzymes and cathepsin G to break down (bacterial) proteins, lysozyme to break down bacterial cell walls, and myeloperoxidase (used to generate toxic bacteria-killing substances). Secretions stimulate the phagocytosis of IgG antibody-coated bacteria.
- *Secondary granules* :
Contain compounds that are involved in the formation of toxic oxygen compounds, lysozyme, and lactoferrin

CELL INJURY

Biochemical mechanisms of cell injury and cell death are —

- **ATP depletion** is critical event in both ischemic and toxic injury
- Oxygen and O_2 -derived free radicals (reactive oxygen species) are bactericidal.
- ↑ intracellular calcium and activation of lytic enzymes—phospholipases/endonucleases/proteases/ATPases
- Cellular swelling (d/t defect in membrane permeability) is the first and consistent manifestation of almost all forms of cell injury.
- **Reversible injury**
Cellular swelling, fatty change on LM. Formation of cytoplasmic blebs, detachment of ribosomes from ER, myelin figures

Features of irreversible injury

- Formation of large amorphous densities in mitochondrial matrix, disruption of cellular membrane
- Profound nuclear changes-- pyknosis (nuclear condensation), karyorrhexis (fragmentation), karyolysis
- *Mechanism of cell death in hypoxic injury is defective oxidative phosphorylation and decreased ATP synthesis.*
- *Fatty change occurs in hypoxic injury and various forms of toxic or metabolic injuries*
- *Membrane damage is the critical event leading to lethal (irreversible) cell death.*
- *Increased cytosolic Ca^{++} is the mediator of biochemical and morphological alterations leading to cell death.*

APOPTOSIS

- Also k/as **Programmed cell death**.
- Normal process by which existing epithelial cells of skin are replaced by new one is an example of apoptosis.
- Physiological programmed destruction of cell is seen during embryogenesis including implantation, organogenesis, involution, and metamorphosis
- In the initial stages cell membrane remains intact on LM. **Annexin-5** attaches to cell surface.
- EM : Chromatin condensation is **the most characteristic feature of apoptosis**.
Cell shrinkage, cytoplasmic blebs and apoptotic bodies
- *On histology intensely eosinophilic cytoplasm with dense nuclear chromatin fragments. Chromatin fragments visualised by electrophoresis as "DNA ladders" pattern.*
- *Methods to detect apoptosis / to label DNA breaks are— ISEL, TUNEL, dTUP, ISNT (CD - 94 is a marker)*
- **P-53** is an apoptosis promoter gene while **bcl-2, Bcl-x, Mcl-1** are apoptosis inhibitor genes (remember p is promoter)
- **Caspase** are cysteine protease enzymes involved in apoptosis. Caspase 8,9 are initiator while 3,6 are executioner.
- *Apoptosis (in contrast to cell necrosis) does not elicit inflammation.*
- *Organelle playing pivotal role in apoptosis is mitochondria. Apoptosis is the result of increased mitochondrial permeability and release of pro-apoptotic molecules.*
- *In the cytoplasm enzyme cytochrome -c binds apaf-1 and activates caspase 9a*
- *Other proteins involved in apoptosis are — FADD (Fas associated death domain), FLIP*
- *Factor which prevents apoptosis of memory cells — NGF*
- *Ladder pattern is seen in apoptosis while smear pattern is seen in cell necrosis.*

CELL NECROSIS

- Chromatin fragments show "Smeared" pattern
- 5 types

Type	D/to	Seen in
◦ Coagulative (M/c type)	Irreversible ischemia	Heart (1st wk of MI), kidney, liver, spleen, early gangrene etc.
◦ Liquefactive/colliquative	Ischemia, focal infections	Brain infarcts, Abscess cavity, wet gangrene
◦ Caseous	Caseation	Tubercular granulomas
◦ Fat necrosis	Trauma, liberation of lipases (saponification)	Acute pancreatitis, Traumatic fat necrosis of breast
◦ Fibrinoid	Immune mediated	Vasculitis (PAN), HTN

- ➔ A localized area of coagulative necrosis is called an infarct.
- ➔ Coagulative necrosis can be seen in all organs except brain.

CALCIFICATION

Pathological (heterotopic) calcification is of two types

Dystrophic calcification

- Seen in dead/ degenerated tissues, serum Ca^{++} levels are normal
- It may be either intracellular or extracellular
 1. *Intracellular* --- In mitochondria of dead tissue
 2. *Extracellular* --- In matrix vesicle
- E.g. RHD, atheroma, aneurysm, lymph nodes, damaged heart valves, Psammoma bodies

Metastatic calcification

- Seen in normal tissue, a/w hypercalcemia.
- Affects kidneys (nephrocalcinosis), GIT, lungs, arteries etc. Starts in mitochondria.
- E.g. hyperparathyroidism, multiple myeloma, sarcoidosis, Paget's disease, William's syndrome, vitamin D toxicity, breast cancer, aluminium intoxication as in milk alkali syndrome.

Hyperplasia

- Increase in the number of cells in an organ or tissue, which usually results in increase in volume

- Cells capable of DNA synthesis undergo hyperplasia.
- Examples
 - Physiological : Hyperplasia of female breast, uterus under hormonal influence
 - Proliferation of residual liver cells after partial hepatectomy, BPH.

Hypertrophy

- ↑ in the size of cells, which usually results in ↑ in size of an organ.
- Cell enlarge but no new cells.
- Examples
 - Physiological : Skeletal m/s hypertrophy in response to exercise
 - Hypertrophic cardiomyopathies d/to chronic volume overload

- ➔ Hypertrophy and hyperplasia both occur in --- Uterus in pregnancy

AGING

- Most widely accepted theory is --- Damage to cells by accumulation of free radicals in tissues. Species with longer life span produce more SOD (superoxide dismutase), an enzyme that inactivates oxygen free radicals
- Aging is also a response to accumulated damage to DNA (Random mutations in the DNA of somatic cells)
- Changes in the amounts of certain GAGs (glycosaminoglycans)
- M/c cause of cancer with ageing --- Telomerase reactivation
- There occurs 'telomere shortening' and ↓ in size of chromatin with age d/to ↓ telomerase activity.

Cilia, Stereocilia & Microvilli

Free surface of epithelial cells show 3 types of specialization in some organs of body -

- *Cilia*
Hairlike, motile processes which propel liquids, mucous or foreign bodies in respiratory and female genital tract
- *Microvilli (Brush border cells)*
They ↑ surface area for absorption. Numerous in GIT and are also present in PCT and DCT of nephrons.

• Stereocilia

Static (non-motile) cilia, found in epididymis. They act as sensory receptor in macula & cristae of vestibular apparatus.

Cells: Types

Type	Part of cell cycle in which the cells are found	Properties	Examples
• Labile cells	G ₁	Actively dividing	Skin, entire resp/GIT/urinary tract cells, stem cells, hemopoietic cells
• Stable	G ₀	Quiescent	Hepatocytes, osteo-/chondro-/fibro-blast smooth m/s cells, endothelial cells
• Permanent		Non-dividing	Neurons, skeletal & cardiac m/s cells

→ Oval stem cells also k/as hepatic progenitor cells (HPCs) are seen in hepatic regeneration.

CYTOSKELETON OF CELL

Microfilaments

- Composed of contractile proteins mainly actin and myosin
- Form microvilli which increases absorptive surface of cells.

Microtubules

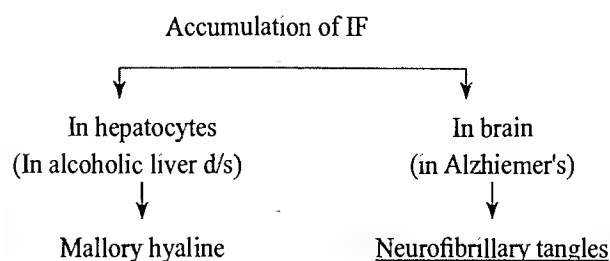
- Composed of **tubulin** protein
- Centrioles, Cilia, Flagella and mitotic spindles contain microtubule
- Role in locomotion of cells
- Defect in organization of microtubules causes impaired sperm motility, Kartagener's syndrome (inhibited respiratory epithelium motility)

Intermediate Filaments

- Mechanically integrate the cell organelles within cytoplasm

- eg. : Keratin, vimentin, desmin, neurofilaments, glial filaments

- Accumulation of IF~



→ **Ubiquitin** is a small protein which degrades many intracellular proteins.

→ **Laminin** is major protein component of glomerular basal laminae (GBM)

→ **Extra-Cellular hyaline** is seen in—Leiomyoma, chronic GN, Arteriosclerosis..

→ **Corpora amylacea** are masses of hyaline seen in prostate, brain & spinal cord in elderly, and old infarct of Lung.

AMYLOIDOSIS

- Amyloid deposits c/b seen in any organ interstitium except CNS.
- **Kidneys** are the most frequently (80%) affected organs. Renal amyloidosis is usually manifested by nephrotic range proteinuria, hypoalbuminuria, edema, anasarca.
- Cardiac /f : cardiomyopathy, diastolic dysfunction
- Neurological /f : Peripheral sensory neuropathy, Carpel tunnel syndrome
- Macroglossia : Tongue is large, immobile and indented.
- Spleen : Two patterns are seen -
 - **Sago spleen**: Spleen is not marked. C/S shows translucent, pale, waxy nodules resembling sago grains
 - **Lordaceous spleen**: Splenomegaly is marked. Cut surface shows map like areas of amyloid.
- 95% of the amyloid material consists of fibril proteins, (having Cross- β -pleated sheet structure) remaining 5% are being the P-component and other glycoproteins. P-component is PAS+ve glycoprotein synthesized in liver.

- AL (amyloid light chain) proteins are derived from plasma cells while AA (amyloid associated protein) is synthesized by RES cells of liver.

Amyloid Proteins and Related Clinical conditions

Amyloid protein	Associated clinical conditions
AL (Amyloid light chain protein)	Primary amyloidosis (e.g. multiple myeloma)
AA (Amyloid associated protein)	2 ^o (reactive systemic) amyloidosis and chronic inflammation (TB/ Osteomyelitis/ bronchiectasis), Familial mediterranean fever CTDs (RA, AS, PBC) Cancers (RCC, Hodgkin's d/s)
β_2 microglobulin ($A\beta_2m$)	Hemodialysis associated a~
β_2 amyloid protein $A\beta$	Senile cerebral a~, Alzheimer's d/s
Transthyretin (ATTR)	Familial amyloid neuropathies, systemic senile a~
Calcitonin associated (A_{cal})	Medullary carcinoma of thyroid
Islet amyloid peptide (AIP)	Type II diabetes
Misfolded prion protein (PrP_{sc})	Prion associated a~
AANF	Isolated atrial amyloidosis, prion d/s

- In secondary amyloidosis the amyloidosis is derived from — AA (amyloid associated protein)
- Amyloid is stained with Congo red and observed under LM (ordinary light) --- Pink red colour
Polarised light --- Apple green birefringence
- Electron microscopy — amyloid is made up of non-branching fibrils of indefinite length & diameter of 7.5-10 nm.
- X-ray crystallography and infrared spectroscopy demonstrates a characteristic cross- β -pleated sheet structure
- The diagnosis depends on demonstration of amyloid deposits in tissue.
- M/c biopsied organs are kidney, rectal or gingival tissues.
- M/c familial form of amyloidosis is familial medeterian fever.
- Pinch purpura is seen in --- 1^o (primary) systemic amyloidosis,

Staining characteristics

Stain	Appearance
1. H & E	--- Pink, hyaline, homogenous extracellular structureless material
2. Crystal /methyl violet	--- Metachromatic rose pink

- Congo red --- LM: red colour (or pink red)
[Confirmatory method] Polarized light: Apple green birefringence
- Fluorescent stains --- Yellow fluorescence
Thioflavin T/S under UV-light
- Immunohistochemistry --- Positive immunoreactivity, (antibodies against fibril) used for classification
- Non specific stains
 - Standard toluidine blue --- (in polarized light: dark red birefringence)
 - Alcian blue --- Blue-green (for MPS content) amyloid

VASCULAR STASIS

Chronic venous congestions (CVC)

CVC Lungs

- Occurs in Lt. heart failure (rheumatic MS)
- Gross: **Brown induration of lungs**, Siderosis
- Histo: *Heart failure cells* are seen containing hemosiderin (alveolar macrophages) which is stained by prussian blue.

CVC Liver

- Occurs in Rt. heart failure (sometimes d/to IVC/ hepatic vein occlusion)
- Gross: **Nutmeg liver**
- Histo: Centrilobular fibrosis resulting in cardiac cirrhosis

CVC Spleen

- Occurs in Rt. heart failure (& in portal HTN)
- Congestive splenomegaly
- Histo: *Gamma- Gandy bodies /siderofibrotic nodules*

Thrombi

- Arterial (white) thrombi
Platelets mass is main constituent of thrombus.
- Venous thrombi
A fibrinous tail is formed which traps the RBC & forms "Red tail" d/to sluggish blood flow

Red & Pale infarcts

• Red (haemorrhagic) infarcts

Are wedge shaped. Seen in **lungs** (also in ovary, testes, small intestine, heart). D/to venous occlusion.

• Pale (white) infarcts

Sharply demarcated white infarcts are seen in spleen, kidney, liver, lower limbs, brain. D/to end artery occlusion.

→ Pathognomonic cytological change in all infarcts is ischemic coagulative necrosis.

→ Occlusion of portal vein or its branches generally do not produce ischaemic infarct but instead reduces blood supply to liver parenchyma causes non-ischemic infarct called **Infarct of Zahn**.

→ Lines of Zahn are seen in — Non-ischemic infarcts of liver

→ Splenic infarcts are seen in — CML, SABE (when cardiac valve vegetations embolize), Myeloproliferative d/s & RA.

→ White infarcts are seen in — Splenic artery occlusion.

→ Digital infarcts are seen in — Infective endocarditis.

Gamma Gandy bodies

• Formed by deposition of **iron + Ca⁺⁺ salts** in connective tissue / elastin of spleen.

• Seen in

- Congestive splenomegaly (Diffuse fibrous scarring of alcoholic/pigment cirrhosis)

- CVC spleen

- EHPVO, idiopathic portal vein thrombosis, pyophlebitis

- Ca stomach / pancreas

• Cru-cut hair lesions with Gamma-Gandy bodies is seen in - **Sickle cell anemia**

• Cru-cut hair lesions without Gamma-gandy bodies

- Thalassemia (m/c cause of Cru-Cut hair lesion / Hair on end appearance)

- Severe iron deficiency anemia.

- Other hemolytic anemias

INFLAMMATION AND HEALING

Sequence of events in acute inflammation

1. Margination: accumulation of leukocytes in lumen
2. **Rolling**: leukocytes adhere transiently to endothelium
3. Adhesion:
4. Transmigration across endothelium (**Diapedesis**)
5. **Chemotaxis** — Extravasated WBCs emigrate uni-

directionally toward the site of injury (locomotion along chemical gradient)

Endothelial molecules & their role

Endothelial molecule	Leucocyte receptor	Major role
P-selectins	Sialyl Lewis X (PSGL-1)	Rolling (neutro, lympho, mono)
E-selectins	Sialyl Lewis X	Rolling, adhesion to activated epithelium
ICAM-1	CD11/CD18 (Integrins)	Adhesion arrest, transmigration
VCAM-1	VLA-4	Adhesion

Acute Vs Chronic Inflammation

• Acute inflammation is c/ by — Vascular changes, edema and largely neutrophilic infiltration. Most characteristic feature is — Vasodilation and vascular permeability leading to protein rich exudate.

• In acute inflammation, endothelial retraction leads to early transient ↑ in permeability, which is the m/c mechanism of vascular leakage.

• Chronic inflammation is c/ by —

1. Infiltration with mononuclear cells (macrophages/ lymphocytes/plasma cells)
2. Tissue destruction
3. Attempts at healing by connective tissue replacement of the damaged tissue accomplished by proliferation of small vessels (angiogenesis) and fibrosis.

• Some characteristic cells in inflammations

→ Chronic inflammation is c/by infiltration of lymphocytes & macrophage but in chronic endometritis there are **Plasma cells**.

→ Acute appendicitis — Neutrophils are found in m/s layer

→ Receding appendicitis — Eosinophils are found in m/s coat

In inflammation, mediators of

• Pain: **IL-1, IL-6, TNFα, Bradykinin, PG (F₂ & E₂)**
Serotonin, AMP, Ach, Potassium

• Fever (hyperthermia):

IL-1, IL-6, TNF, CNTF, IFNα, PG

• Eosinophils secrete: MBP, hydrolases, reactive O₂ species

• Platelets secrete: Serotonin

• Chemotaxis Mediator: LTB₄, IL-8, C5a

Leukokinin, Lysosomal cationic protein

Inflammatory Mediators

Category	Mediator	Source	V/d	P	C	Other effect	
	Histamine	Mast cells basophils, platelet	-	++	+	-	WBC adhesion
	Serotonin	Platelets	-	+	-	-	Arteriolar constrict ⁿ
	PAF	Platelets,			+		Broncho- constrict ⁿ
	Bradykinin	Plasma kininogen	+	+	-	-	Pain
	PG	Cell memb. PL	++	-	-	-	Pain
	LT- B ₄	Leucocytes	-	-	+	+	
SRS-A	LT- C ₄ D ₄ E ₄	Leucocytes, mast cells	-	+	-	-	
Anaphylo toxins	C _{3a}	Liver	+	+	-	-	
	C _{5a}	Liver	+	+	+	+	

[V/d = Vasodilatation, P = Permeability, C = Chemotaxis]

IMMUNITY

Important Surface Antigens/CDs on Cells

CD	Found on (T ^h Cell distribution)	Function
CD1a		Thymocyte & Langerhans cell associated
CD3	Pan T-cell marker	T cell receptor
CD4	T helper-inducer cells, macrophage	Binds to MHC class II, +ve in Mycosis fungoides
CD5	----	Mantle cell lymphoma
CD8	T cytotoxic-suppressor cells	Anti-viral & anti-cancer properties, binds MHC-I
CD10	Immature B cells	CALLA antigen, found in ALL
CD13,14	Monocytes	
CD16, 56	NK cells	Anti-viral
CD19	Pan-B cell marker	Appears early in B-cell maturation
CD20/21/22	B cell markers	CD 21 is complement receptor (CR2)

CD25	Marker of T, B & macrophage	Marker of HCL
CD33,13	Most sensitive myeloid cell marker	
CD34	Hematopoietic progenitor cells	"Stem Cell" marker
CD38	Plasma cells	Multiple myeloma marker (also CD-33)
CD45	Leukocyte common antigen	Pan leukocyte marker, for malignant lymphoma
CD45RO	Memory T-cells	Subset of T cortical thymocytes
CD30	Marker for Hodgkin's ds	LP -ve
CD117	Most specific myeloid cell marker	Marker for myeloid lineage in AML, CML, blast crisis, granulocytic sarcoma from left ventricle.

- CD1 to 8 are T-cell markers except CD6.
- CD 19,20,21 are B-cell markers.
- CD marker most specifically a/w GIST — CD117
- In Mantle cell lymphoma CD 19, CD 20, CD 43, & CD 5 +ve but CD 23 -ve.
- In Burkitt's lymphoma CD 19, CD 20, CD 10 +ve.

[for details see hemato section]

Important Autoantigens & Autontibodies

Autoantigen	Autoantibody	D/s
Actin	Anti SM, anti mitochondrial	Chronic active hepatitis, PBC
Desmin		Crohn's d/s
F-actin	ANA (type 1), Anti-LKM (Type 2), Anti-SLA (Type 3)	Autoimmune hepatitis,
Thyroglobulin		Autoimmune thyroiditis
Th.peroxidase		Hoshimoto thyroiditis
Thyrotropin receptor	LATS	Grave's d/s
	Anti-parietal cell Ab	Chronic atrophic gastritis
Intrinsic factor-I	----	Pernicious anemia
Synaptogranin		LAMES
SOX-1		Vitiligo

Trafficking Molecules in inflammatory d/s

Type of inflammation	D/s	Key Effector cell
Acute	MI	Neutrophil
	Stroke	Neutrophil
	Ischemia -reperfusion	Neutrophil
T _H 1	Atherosclerosis	Mono, T _H 1
	RA	Mono, T _H 1, neutro
	Psoriasis	T _H 1
	Crohn's	Gut homing Mono, T _H 1
	Type 1 DM	Mono, T _H 1, CD8
T _H 2	Asthma	Eosino, mast, T _H 2
	Atopic dermatitis	Skin homing T _H 2

W/c Locations for

	In LN	In Spleen
B-cells	Germinal follicles	Mantle zone (red pulp)
T-cells	Paracortical (in cortex)	Periarteriolar sheath in white pulp
Histiocytes	Sinuses	Cords of Billroth

Monocyte - macrophage lineage derivatives

These cells form part of RES & are concerned with phagocytosis

- Kupffer cells of liver
- Microglial cells of CNS
- Langerhans cells of skin
- Dendritic cells in lymphoid tissues
- Epithelioid cells & Multinucleated giant cells
- Histiocytes of connective t/s.

Giant Cells : types

Multinucleate cells made by fusion of macrophages

Type of Giant cell	Seen in
1. Foreign body type	Chronic infective granulomas
2. Langhans' type	TB, sarcoidosis
3. Touton's	Xanthoma (vacuolated cytoplasm+)
4. Aschoff cells	Rheumatic fever/carditis
5. Reed-Sternberg cells	Hodgkin's lymphoma
6. Osteoclasts	Osteoclastoma

→ Tumour giant cells (as in HCC, soft tissue sarcomas) are not derived from macrophages but are formed from dividing nuclei of neoplastic cells.

→ Antigen presenting cells (APCs) are — macrophage subpopulation (Dendritic cells in lymphoid tissues, Langerhan's cells in epidermis, NK-cell & T-cells)

MHC Antigens (HLA system)

○ MHC Antigens (HLA system)

○ MHC-I is expressed on all cells. On viral infection, MHC-I lysed sensed by NK cells produced by perforins & granzymes.

○ 3 classes of MHC (or HLA) antigens are there:

	Class-I	Class-II	Class-III
Locus	HLA-A, B, C loci on chromosome 6	HLA-D (DP, DQ, DR)	Complements
Found on	All nucleated cells & platelets (but it is not present on RBCs)	Antigen presenting cells (+ monocyte/macrophages, & B cells)	Complement (C ₂ , C ₄ TNF _β HSP-70)
Func ⁿ	Endogenous (viral/tumour) Ag to T _C cells (CD8 cells)	Exogenous Ag to T _H cells (CD4 cells)	Encode for enzyme 21 hydroxylase

→ Genes for major histocompatibility antigens (or HLA antigens) are located on chromosome 6p (short arm of 6).

→ MHC-I allele presents the antigen to T-cells through proximal portion of α-chain.

→ CD8 T-cells, kill in context of MHC-I while CD4 cells kill in context of MHC-2 [Rule of 8; 1x8 = 8 or 2x4 = 8].

→ Best APCs are— Dendritic cells (most imp) and Langerhan cells.

→ NK cells are MHC unrestricted.

→ Minor histocompatibility Ag are also located on chromosome 6

SOME IMP. HLA ASSOCIATIONS

HLA	Seen in
A1	Hodgkin's d/s
A3	Idiopathic hemochromatosis
B5	Behcet's syndrome, UC, PCOD
B8	Nasopharyngeal carcinoma
B27	Psoriasis, Ankylosing spondylitis, Acute anterior uveitis, Reiter's d/s, Reactive arthritis

B47	Congenital adrenal hyperplasia
DR2	Narcolepsy
DR2/DR3	Grave's d/s
DR3	SLE,RHD, CAH (chronic active hepatitis), Sjogren's syndrome
DR4	RA, Pemphigus
DR5, B5	Behcet's syndrome
DQw1	LL (lepromatous leprosy)
DQ2	Coeliac Sprue

→ NIDDM is NOT a/w HLA.

Types of Graft Rejection

	Hyperacute	Acute	Chronic
Time	Immediately within 48 h (rare now a days)	Weeks - upto 6 mo. or after withdrawal of immuno- suppressive Rx	occurs years later/ may follow repeated acute rejection
Due to (Mediated by)	<u>Preformed antibodies</u>	CD4, CD8 T cells	Ab, immune complexes
		Acute cellular rejection (M/c type)	Acute humoral rejection
Type of HS Reactⁿ	Type II	Type IV	Type I or II
E.g.	Seen in multi-transfused pt., multiparous women, previous transplant, vascular anastomosis.		<u>Renal allograft</u> may develop glomerulonephritis.
T/t	Avoidable by HLA-matching	Immunosuppressives	Resistant, occurs after all types of transplanatation.

- First liver transplantation was done by Starzl.
- 1st lung transplantation was done by Hardy.
- 1st autologous renal transplantation was done by Hardy.
- 1st succesful cornea transplantaⁿ done by Edward Jig.

- HLA matching can match the major antigens (MHC Ag) not the minor antigens, so immunosuppression is required even after HLA matching.

- A cadaveric donor is someone who has recently died. A cadaveric donor is required for the transplantation of kidney.

• Order of immunogenicity ---

BM > skin > kidney > liver > Heart. (i.e. BM transplantation require maximum HLA matching)

- Triple therapy immunosuppression for post renal- transplant patients include --- Cyclosporine + Aza + pred

• Malignancy After Transplantation :-

After transplantation there is increased risk of malignancy

- Skin cancers esp **SqCC** are m/c type. Others are :

BCC, malignant melanoma

- NHL

- Ca cervix.

• Types of grafts

1. Autograft : From one part of body to another. Most of the skin grafts.
2. Syngenic graft : Graft b/w identical twins
3. Allograft : B/w 2 individuals of same species.
4. Xenograft : B/w 2 different species. Chances of graft rejection are maximum.

- Best donor for allograft --- Identical twin.

• Organ specific features of Graft rejection

1. Kidney --- Glomerulosclerosis and tubular atrophy
2. Pancreas --- Acinar loss & islet destruction
3. Heart --- Accelerated coronary artery diseases.
4. Liver --- Vanishing bile duct syndrome (bile ductopenia, paucity of ducts)
5. Lungs --- Obliterative bronchiolitis.

• Graft versus Host D/s (GVHD)

1. Also k/as *Runt d/s*.
2. Characterised by jaundice, GI lesions, skin rashes.
3. BM & liver transplants are most commonly a/w GVHD. GVHD is not seen with /rare with renal transplant.

→ *M/c indication for liver transplantation --- Chronic liver failure, biliary atresia (in children).*

→ *M/c GN in transplanted kidney --- MPGN type-II.*

→ *Type of transplant with the best graft survival --- Autograft*

→ *Commonest tissue transplant with best overall survival ---- Corneal transplant because of avascularity.*

→ *Factors that improve graft survival ---*

ABO compatibility, absence of anti-HLA antibodies, HLA compatibility b/n D-loci.

→ *All types of allograft are susceptible to chronic rejection & it is the major cause of allograft failure. Both MHC class I & II (Class II > I) have role in allograft rejection.*

HYPERSENSITIVITY REACTIONS : TYPES

	D/to or mechanism	Pathogenesis	Seen in
I	IgE Ab ↓ Mast cells degranulation ↓ Release of mediators	Localised (ATOPY) (Run in families, have genetic predisposi ⁿ)	Allergic conjunctivitis Allergic rhinitis, Asthma, Food allergy, Allergic dermatitis, Hay fever, PK (Prusnitz Kunster) reac ⁿ Theobald Smith phenomena
		Systemic	Anaphylaxis
II	Antibody mediated ↓ Antigen is FIXED on cell memb/ connective tissue	Kill the target cells	<i>Complement MAC (C5-C9) mediated</i> → <i>lysis of target cell</i> Mismatched BT, AIHA, Granulocytopenia, Thrombocytopenia Pernicious anemia, Pemphigus vulgaris, Good pasture's syndrome, Rheumatic fever <i>Cells with Fc receptor (NK/macro/neutro) mediate</i> → Ab dependent cellular cytotoxicity (ADCC)
		<i>Auto-Ab vs target cells</i>	MG, Grave's d/s
III	Immune complex d/s ↓ Settles down in skin, vessels, LN, kidney, joints, spleen ↓ Thrombi forma ⁿ in vessels & tissues	Antigen is SOLUBLE [NOT fix]	Local Arthus reaction, (Farmer's lung, Acute PSGN, Reactive arthritis, GN-Syphilitic / membranous) Systemic Serum sickness, SLE, PAN, RA, drug induced AIHA
IV	T Lymphocytes	CD ₄ T cells → Classic Delayed HS CD ₈ T cells → Cellular cytotoxicity	Immune granulomas (TB, leprosy, LGV, Syphilis, Sarcoidosis, Montenegro test for Leishmaniasis) Rheumatoid arthritis, Multiple sclerosis, Type 1 DM, GBS, Patch test for contact dermatitis/poison ivy dermatitis, John Mote cutaneous basophil reac ⁿ <i>Direct cell mediated cytotoxicity</i> Graft rejection, tumour cell lysis, virus infected cell lysis

- R_x of HS reaction Adrenaline (DOC), steroids, antihistaminic
- DOC for Type-II, Type-III, Type - IV → Steroids

NK Cells (Natural Killer Cells)

- Also k/as killer cells/large granular lymphocytes.
- NK cells & complements are part of innate immune response.
- 1st line of defense against virus laden & cancer cells.
- Azurophilic granules (large granular lymphocytes) +nt.
- Lyse the cell **without** prior sensitization (cytotoxicity is not MHC restricted).
- Receptors (TCR) -nt but antigens present **CD16 & CD56**.

CD 4 Cells

- Formation of memory helper T cells
- Activation of cytotoxic T cells (CD4 TH1)
- Activation of B cells to produce antibodies (CD4 TH2)

Difference between T - Cell and B - cell

	T - Cell	B - cell
• Old name	<i>Small lymphocyte</i>	<i>Large lymphocyte</i>
• % in blood.	70%	20%
• In Bone marrow.	rare or -nt	Numerous
• In LN	85%	15%
• In Spleen.	15%	35%
• In Thymus.	90%	10%
• Rosettes	E - rosettes or (sheep RBC (<i>SRBC</i>) <i>rosette</i>)	<i>EAC - rosette</i>
• Location		
• In Lymph Node	Perifollicular (Paracortical)	Germ centre, medullary cords.
• In spleen	Peri-arteriolar	Germinal centre, mantle layer
• In Payer's patches	Peri-follicular	Central follicles.
• Surface marker	Ag - receptors.	Surface Ig, Fc receptor, complement receptor.
• Marker	CD- 3 (Pan - T cell marker present on all T-cells) Surface smooth	CD-19 (Pan-B cells marker) (+nt on all B cells) Surface Rough with projections
• Multiplication	T-cells undergo blast transformation (evidenced by ↑ DNA synthesis) on treating with mitogens ex- phytohemagglutinin or concavalin A	B-cell undergo transformation with bacterial endotoxins.

→ *Intestinal epithelium is rich in T-cells*

→ *Most potent activator of T cells --- Mature dendritic cells*

INFECTIONS

TYPHOID

- Longitudinal ulceration of Peyer's patches
- Stricture are rare/not seen
(So intestinal obstruction is also rare)
- Rose spots are seen in 2nd week.
- M/c complication - perforation /ulcers which are seen during 3rd week.
- Mainly involves ileum and sometimes colon. Blunted villi are found
- Erythrophagocytosis + (erythrophagia) and monocytosis
- Leucopenia +, relative bradycardia
- Pea-soup diarrhea in early phase later on constipation.
- Minimum infective inoculum of *s.typhi* is 10^2 - 10^5 bacilli.

Ulcers in

TB	Transverse, multiple, circumferential ulcers with strictures Mesenteric LN involved.
Crohn's d/s	Longitudinal ulcers
Amebic ulcers	Flask shaped ulcers (Irregular large confluent ulcers)

H. PYLORI

- Also k/as *Campylobacter pylori* or *gastrospirillum*
- Bacterial Characteristics**
 - Gram - ve spiral organism (helical in vivo, rod-like / comma-shaped in vitro, coccoid on old cultures)
 - +ve staining with Giemsa, silver &, Warthin-starry
 - Resistant to physical/chemical injuries
 - Motile by 4 unipolar (lophotrichate) flagella
 - Oxidase⁺ Catalase⁺ Phosphatase⁺, produces H_2S
 - Strongly urease positive which forms NH_3 and plays role in colonization.
- Micro aerophilic/obligatory anaerobic in culture. Require 5-20% CO_2 , pH of 6-7, and 37°C temperature.
- It is non-invasive living in the mucous that overlies gastric mucosa. Cag A gene region (pathogenicity island) is a marker of cytotoxicity (cell damage) or vacuolating activity (Vac gene).
- Most infections are acquired in childhood & 80% of individual have antibody to H~ by age 20 year. most of them are asymptomatic. There is *no life long immunity*.
- Pathology**
 - Chronic superficial gastritis, monocytic & neutrophilic infiltration of mucosa & injury to epith. cells.

- Somatostatin producing D-cell are ↓ed.
- Gastrin producing G-cells are unchanged.

o H. pylori is a/w

- Peptic ulceration : **Duodenal ulcers** > gastric ulcers (in prepyloric area or body of stomach)
- Gastric MALT lymphomas
- Gastric adenocarcinoma
- Type B / antral / chronic atrophic gastritis d/to achlorhydria.
- Non-ulcer dyspepsia
H. pylori probably play no role in lymphocytic gastritis or in eosinophilic gastritis
Old age, Poor SES is risk factor for development of d/s

o T/t

- Standard **triple therapy** regime is bismuth subsalicylate + tetracycline + Metro [Mnemonic: TBM]
- Quadruple therapy** - PPI + tetracycline + CBS + Metro
- Triple therapy with :- Pantoprazole + Amoxicillin + Clarithromycin is a popular regime.**

- Success of t/t is assessed by → ^{14}C urea breath test.

o Diagnostic tests

Rapid urease	90%	95%	Simple, reliable
Histology	96%	96%	
Culture	70%	100%	Most specific
1. Serology/ ELISA (Anti-IgG)	95%	90%	Best epidemiological tool
2. ^{13}C /Urea breath test	95%	99%	

o Serology :

- Does not differentiate b/n active & remote infection (titres ↓es slowly after eradication)
- Epidemiological tool*
- Now widely used for routine detection, m/c done by ELISA method
- Anti urease Ab detection is specific for type I

H. Heilmannii

- Zoonotic, weakly urease +ve organism which can not be cultured in vitro.
- Causes gastritis & spontaneous petechial hemorrhages which resolve spontaneously.
- Bismuth alone is effective in treatment.

HEPATITIS B (HBV)

Serological Markers in

	HBs Ag	HbeAg	Anti-HBs	Anti-HBe	Anti-HBc IgG
Acute infection	+	+	-	-	+
Chronic infection	+	+	-	-	+++
Recent HBV infec ⁿ , cured	-	-	++	+	++
Past HBV infec ⁿ , cured	-	-	+	-	+
Healthy carrier	+	-	-	+	+++
Recent HBV vaccination	-	-	++	-	-
Recovery from HBV	-	-	+	+	+

- **Dane particle** is complete hepatitis B virus (double wall spherical structure) but it does not contain delta-antigen.
- HBs Ag is produced in considerable excess & may accumulate in smooth ER producing the characteristic "Ground glass" hepatocytes. Excess HBs Ag also appears in serum.
- Using immuno cytochemistry **HBc Ag is localised predominantly in hepatocyte nucleus** (HBc Ag is not + nt in blood), whereas HBs Ag is found in Liver cell cytoplasm.
- Infants born to HBsAg +ve mothers should receive both HbIg & HB vaccine i/m at separate sites within 12 hour of birth followed by 2nd & 3rd dose of vaccine at 1 & 6 mth respectively.

HBs - Ag (Australia Antigen)

- First serological marker to appear in blood after exposure to HBV. Detectable even before the rise of SGOT/PT & onset of clinical illness.
- It appears in blood wks-mths after exposure, reaches peak within few wks, persists throughout icteric/symptomatic course of d/s & declines / disappears with clinical recovery (usually within 2 mths)
- In chronic infection HBs Ag does not disappear but in fact rises to high titre (which usually persist for life time)
- Four distinct antigenic subtypes of HBs Ag exist these are useful in epidemiological studies.

Hbe-Ag

- Invariably +nt in acute phase & is **marker of infectivity** (bec HBV-DNA is circulating in blood & active intrahepatic viral replication +nt). HBV DNA is also an indicator of infectivity & replication
- A/w ↑ transaminases level & symptoms
- Disappearance of Hbe ag coincides with fall of transaminase level in blood. It is followed by appearance of anti-Hbe Ab.
- HbeAg is the **major predictor of vertical transmission**. Mothers who are HbeAg +ve are more likely to transmit the disease to fetus (HBV-DNA is also but less important).

Anti-HBc

- Appears 1-2 wk after appearance of HBs Ag. It is the **first antibody to appear in blood**.
- D/g of acute infection rests on identification of IgM anti-HBc Antibodies.
- Because most individual often present late in the course of d/s when HBs Ag has disappeared or very low in titre, measurement of the **IgM anti HBc is the most valuable (best) serological marker of acute HBV infection**.
- Only serum marker during window period (interval b/n disappearance of HBs Ag & appearance of Anti HBs)
- IgM proportion soon declines, after 6 mth it is mainly IgG Anti HBc which persists for years. It remains life long and serves as a useful indicator of prior infection with HBV (past/remote infection), even after other markers become undetectable, it is invariably present in carriers (*In persistent infection it is + nt along with HBs Ag*)

Anti - HBe

- Indicates recovery process from infection
- Presence of Anti-HBe in chronic carrier is a/w relatively low infectivity & good prognosis.
- Absence of Hb-e Ag in presence of Anti-Hbe seems to be protective against transplacental transmission to fetus from mother.

Anti-HBs

- Appears in serum during convalescent phase.
- It is a neutralizing, protective Ab largely responsible for immunity to re-infection.
- Presence of Anti HBs without any other marker indicates immunity following **vaccination**.

Comparative features of hepatitis viruses

Type	HAV	HBV	HCV	HDV	HEV
Virus genome	HAV, 27nm ssRNA	HBV, 47nm partially dsDNA	HCV, 30-60nm ssRNA	Circular defective ssRNA	HEV, 32-34nm ssRNA
Family	Hepato (Picorna)	Hepadna	Flavi	Delta	Calci
Modes of infection	Fecal-oral	Percutaneous perinatal, Sexual	transfusion, intranasal cocaine abuse	Percutaneous	Fecal-oral
Age	Children	Any	Adults	Any	Young adults, pregnant females
IP (days)	15-45	30-180	15-160	30-180	15-60
Carrier state	Nil	Common	+	Nil (with HBV)	Nil
Disease	Infectious, hepatitis	Serum hepatitis	-	-	Fulminant hepatitis in pregnancy
Oncogenicity	-	↑ risk of HCC	+	-	-
Chronicity	-	+(1-10%)	+(50-70%)	-	-
Prognosis	Excellent	worse	mod	poor in chronic	good
A/w	-	PAN	EMC	+	
T/t	-	INF α , Lamivudine	Ribavarin + INF α	+	+

- Hepatitis virus with significant (maximum) perinatal transmission ---HBV
- M/c cause of transfusion associated hepatitis --- Hepatitis C
- Among all hepatitis viruses only HBV is DNA virus other hepatitis viruses are RNA viruses.
- HBV belongs to hepadna viride family & contains double stranded circular DNA (remember - HepaDNA)
- Most epidemics of hepatitis are caused by---Hepatitis E in adults & Hepatitis A in children
- M/c cause of fulminant hepatitis in pregnant women (or a/w high mortality)---Hepatitis E
- Anti-LKM antibodies are seen in hepatitis

LKM 1 → Type II autoimmune hepatitis

LKM 2 → Drug induced hepatitis

LKM 3 → Chronic hepatitis D

- Autoimmune hepatitis

type I is a/w ANA,

type II is a/w ALKM-I and ACL-I

- HBsAg is the 1st marker detectable in serum.
- IgM anti-HBc is the best marker of acute infection; only marker during window period.
- HBeAg is marker of infectivity/replication and major predictor of vertical transmission
- HBe Ag is qualitative marker while HBV DNA polymerase is quantitative marker of acute infection.
- Anti-HBs is the Marker of protection. It is the only marker to appear after hepatitis B vaccination

CNS

Part of brain affected in...

- Hippocampus

Is the m/c site of Negri bodies is neurons in brain (found in Rabies). Hirano bodies are seen in Alzheimer's d/s. It is the part of brain most vulnerable to ischemia.

- Mammillary bodies

M/c affected in Korsakoff's psychoses

Basal ganglia

Site of brain involved in Wilson's disease, Kernicterus.

- In Kernicterus bilirubin seeps into neurons and affects Basal ganglia, hippocampus & auditory bodies.
- Lewy bodies are found in substantia nigra in remaining neurons (not in affected neurons) in parkinsonism.
- Duret hemorrhages are seen in brain.
- Durck granulomas are seen in brain in cerebral malaria.
- Retraction balls are seen in brain in axonal injuries.

Cells of brain

Neurons

Stable cells, no regeneration. 4 classes are there:

1. *Unipolar* : Fetal neurons, mesenchyme nucleus of trigeminal nerve.
2. *Pseudo-unipolar* : above neurons if function as bipolar. E.g. DRG, sensory ganglia of CN.
3. *Bi-polar* : 1st neuron of retina, Ganglia of 8th CN.
4. *Multipolar* : Most neurons in brain, all motor neurons, internuclear neuron.

Neuroglia/glia cells

Support, maintain and repair damaged neurons

Types	Function
1. <i>Astrocytes</i>	Foot process of astrocytes form BBB (endothelium derived), also involved in metabolism of neurotransmitters. Helps in gliosis (gliosis is a histological indicator of CNS injury)
2. <i>Oligodendrocytes</i>	Myelin synthesis in CNS
3. <i>Schwann cells</i>	Myelin synthesis in PNS (neural crest deriv)

Microglia

Derived from mesoderm (monocyte lineage). They synthesize complex granular corpuscles / *gitter cells* (*Hortega cells*) by phagocytosis.

- Fibroblasts are not found in brain (there is no fibrosis in brain).
- Gliosis is an indicator of CNS injury.
- Brain cells in decreasing order of susceptibility to ischemia: Neurons > oligodendrocytes > astrocytes.
- Rods & cones in retina are 1st order neuron in optic pathway.

BERRY'S ANEURYSM (Saccular aneurysm)

- M/c type of intracranial aneurysm
- Defect lies in muscle coat and intimal elastic lamina.
- Most frequent cause of clinically significant SAH is rupture of Berry aneurysm.
- Risk more in females. Risk ↑ in patient with --- EDS type IV, NF-1, AD PKD, Marfan's syndrome, FMD, Co A
- Predisposing factors --- Smoking, HTN
- *Location*
Junctions of ACA with anterior communicating artery 40% (commonest site) > PCA with ICA 20%.
- *T/t* -
To prevent vasospasm after surgical clipping, **triple H therapy** (induced hypertension, hypervolemia & hemo dilution) is initiated at the first sign of vasospasm

HYPERTENSIVE BLEED

- Occurs in basal ganglia (putamen, globus pallidus, thalamus), cerebellar hemisphere, pons.
- **The putamen is the m/c site.** Adjacent internal capsule is invariably damaged.
- HTN is the m/c cause of intracerebral (intraparenchymal) hemorrhage.
- Spontaneous rupture of Berry's saccular aneurysms after excluding head trauma is the m/c cause of SAH
- The hallmark of aneurysm rupture is blood in CSF.
- Non contrast CT scan is for more superior than MRI for acute blood loss.
- Cerebral amyloid angiopathy is probably the m/c cause of lobar hemorrhage in elderly.

LACUNAR INFARCTS

- D/to atherothrombotic or lipohyalinotic occlusion of a small artery in the brain.
- Hypertension and age are the principal risk factors
- Deep penetrating arteries and arterioles develop arteriolar sclerosis and may become occluded. that supply basal ganglia and hemispheric white matter as well as the brainstem. Small single / multiple cavitory infarcts results in **lacunes** / lacunar infarcts.
- These are lake like spaces <15 mm wide and occurs in decreasing order in **lenticular nucleus (m/c site)** > thalamus > internal capsule > deep white matter > caudate nucleus > pons

BLOOD VESSELS

Vasculitis :Classification

Large vessel vasculitis	Medium size vessel vasculitis	Small vessel vasculitis
<ul style="list-style-type: none"> Giant cell/ temporal arteritis Takayasu aortitis 	<ul style="list-style-type: none"> PAN Kawasaki 	<ul style="list-style-type: none"> Wegner's granulomatosis (WG) Churg-Strauss syndrome HSP Microscopic polyangiitis Essential cryoglobulinuria Hypersensitivity angitis

- Hypersensitivity vasculitis (cutaneous leukocytoclastic angiitis) affects --- Post capillary venules.
- M/c type of vasculitides --- Giant cell arteritis.
- Coronary involvement is seen in --- Kawasaki disease.
- Visual loss may occur in --- Temporal arteritis and Takayasu's arteritis
- Hypertension is seen in --- PAN & Takayasu
- Neurological insufficiency is seen in --- Takayasu's arteritis

ANCA (Anti-Neutrophilic Cytoplasmic Ab)

Cytoplasmic or c-ANCA

- Proteinase-3 is major target Ag (PR3 -ANCA)

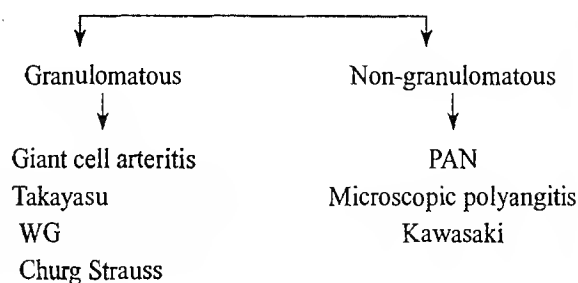
- ↑ in
 - WG (pathognomonic)
 - Active GN

Perinuclear or p-ANCA

- Myeloperoxidase is major target Ag (MPO -ANCA)

- ↑ in
 - PAN, Crescentic/RPGN
 - Churg-Strauss synd
 - Good pasture syndrome
 - IBD, Primary sclerosing cholangitis
 - Microscopic polyangiitis

Granulomatous & non- granulomatous arteritis



	Takayasu	Giant cell	Churg-Strauss Synd	PAN	WG
Synonym	Aortic arch syndrome (Pulsless disease)	Temporal / cranial arteritis	Hypersensitivity angitis	Classic PAN	
Age/Sex	Young females < 40 yrs	F > 50 year	Young	40 yrs	M = F
Arterial predilec ⁿ	Large & medium aortic arch & its branches, CCA, subclavian a. (93%)	Large & medium starts in carotid a & progress towards temporal a.	Medium & small arteries & veins pulmonary a.	Medium & small,	Small arteries & veins
Does not involve	Coronary vessels			Pulmonary a	
CI/F	HTN, eye symptom, higher BP in LL > UL (reverse coarctation)	Jaw claudica ⁿ , eye symptom polymyalgia rheumatica, headache which ↑ with cold/ in night	1. Pulmonary symp. severe asthmatic attacks (m/c symp) 2. Allergic rhinitis	HTN	Respiratory & nasal symptoms with otitis media
Patho	Panarteritis with mononuclear infiltration	necrotising arteritis	GN		Granuloma in URT, Focal necrotizing GN
Lab/f	↑ ESR ↑ Immunoglobulins	↑ ESR	anti-MPO, Peripheral hyper-esosinophilia	↑ p-ANCA HBs antigen in 30% patients	↑ c-ANCA
T/t	Glucocorticoids, & endarterectomy	-	-	-	-

ATHEROSCLEROSIS

- Organisms found to be a/w atherosclerosis --- Chlamydia pneumoniae, CMV, HSV
- Risk factors ↓HDL, homocystinemia, ↑ waist : Hip ratio.
- Intake of saturated fatty acids (SFA) is a/w ↑ risk
- Dietary intake of unsaturated fatty acids ↓es the incidence. PUFA is a/w ↓ risk. However among PUFA, trans PUFA are a/w dyslipidemia and can cause atherosclerosis.
- Typical Vs transplantation(graft) arteriosclerosis.

<i>Typical Atherosclerosis</i>	<i>Graft Arteriosclerosis</i>
- Eccentric Lesion	- Concentric lesion
- Lipid deposits	- No lipid core
- Focal distribution	- Diffuse narrowing.
- M/c sites for atherosclerosis in descending order :
Lower abdominal aorta > coronary arteries > popliteal a. > Descending thoracic aorta > Internal carotid.
- Arteries spared in atherosclerosis are --- Internal mammary a. & radial a. (arteries of upper limb, mesenteric & renal arteries are also spared)
- Hyperplastic arteriosclerosis is seen in kidney, peripancreatic fat, periadrenal fat SI, GB (not seen in heart)
- Commonest location of fatty streaks and fibrous plaques is in **intima**
- Atherosclerotic plaque arise from --- smooth muscle cells of intima. Shear stress is related to ↑ risk
- Atherosclerosis of abdominal aorta is a/w more complications (like aneurysm)
- Hypercholesterolemia is an important independent risk factor.

Abdominal aortic aneurysm

- Abdominal aortic aneurysm is **m/c** type of large vessel aneurysm.
- M/c cause of abdominal aortic aneurysm is **atherosclerosis** (in 90%)
- Atherosclerotic ectasia / aneurysm m/c involves --- Abdominal aorta (typically infrarenal portion).*
- Atherosclerotic stenotic lesion m/c affects --- Coronary arteries (proximal portion of LAD). Atherosclerotic aneurysm are **fusiform** in shape. Involve **infrarenal** portion of abdominal aorta. Contain mural thrombus.
- 95% a/w atheromatous degeneration & 95% occur below renal arteries (**M/c location infrarenal**)
- More common in male & smokers, surprisingly diabetes exerts protective effect.
- Can rupture anteriorly into the peritoneal cavity i.e. intraperitoneal (20%) & more commonly posterior into

retroperitoneal space

Classification

Asymptomatic :

Found incidentally either on Cl/E or on angiography/USG.

Symptomatic without rupture :

Abd/ Back pain, mass in abdomen vertically placed not moving with respiration

T/t

- Surgery is indicated in both asymptomatic (of diam >5.5 cm on USG) & in symptomatic cases (who are medically fit)
- Open surgical repair using PTFE (Poly tetra fluoro ethylene) graft or Dacron graft
- If aneurysm is > 5.5 cm then surgery is TOC**
- Rate of expansion & risk of rupture correlates with
 - DBP
 - Initial aneurysm diameter
 - Degree of obstructive pulmonary disease
- Size of aneurysm correlates best with the risk of rupture
-- about 40% of aneurysm > 5.5-6 cm diam. will rupture within 5 years if untreated

Syphilitic aneurysm

- Seen in tertiary stage of syphilis
- Involve ascending portion of aorta (**m/c site**)
- Saccular in shape. Intima shows **tree-bark appearance**
- Aortic valve involved → AR & '**Cor-bovinum**' (also k/ as bovine heart / core taurinum).

Dissecting aneurysm

- M/c cause is CMN (cystic medial necrosis)
- Seen in elderly & in women during pregnancy.
- Related with Marfan's syndrome, HTN
- *Syphilitic aneurysm involves - Ascending portion of Arch of aorta*
- *Marfan's syndrome involves - Ascending aorta*
- *Atherosclerotic aneurysm involves - Descending aorta (infrarenal portion).*
- *M/c site of tear in aortic injury - descending thoracic aorta. (aortic isthmus just distal to origin of left subclavian a.)*
- *Russmussen's aneurysm involves - Pulmonary artery adjacent to or within a tuberculous cavity*

CVS

MI (MYOCARDIAL INFARCTION)

Molecular Markers in Diagnosis of Acute MI:

- The most sensitive early marker for AMI is myoglobin.
- **CK-MB**: Enzyme elevated within 4-6 hours after MI. It is the gold standard enzyme useful in MI. Peaks at 48 hr.
- Troponin-T (**cTn-T**) is most specific for assessing myocardial damage. cTnT and cTnI have equal myocardial tissue specificity, as well as high sensitivity. Patients with detectable troponin but no CK-MB in the blood may exhibit microscopic zones of myocardial necrosis (**microinfarction**).
- Trop -T normal value is 0-0.1 ng/mL
- Cause of reappearance of CPK-MB after 3 days --- Reinfarction
- **Dressler's syndrome** (Post MI autoimmune pericarditis) C/by fever and pleuro pericardial chest pain seen 1-2 weeks after MI. Responds to salicylates.

Healing of myocardium after MI :

Time	Gross	Light
0-12 hours	-	Waviness of fibers
1 day	Pallor	Coagulative necrosis
1-3 days	Hyperemic border	Neutrophilic infiltration starts
3-4 days	Hyperemic border	<u>Dense</u> neutrophilic infiltration
4-7 days	Pale-yellow	Above + Macrophage appears
7-14 days	Red purple border	Above + <i>granulation tissue</i> (necrotic myocytes removed by phagocytosis).
>2 weeks	Gray white scar	Fibrosis starts
3 weeks		Granulation tissue with a rich vascular network & early collagen deposition

[Remember: Neutrophilic infiltration starts in 2 days, fibrosis starts in 2 weeks, and scar is formed in 2 months]

- M/c late c/c of an acute MI --- Ventricular aneurysm
- M/c cause of death in AMI --- VT leading to VF and death.
- Time after AMI when cardiac muscle is most subjected to rupture is b/w 3 to 7 days when the muscle is softest.
- M/c c/c of acute MI - Arrhythmias (ventricular extra systoles) > LHF > cardiogenic shock > Cardiac rupture.

ENDOCARDITIS

- Most frequent structural lesions a/w endocarditis are TOF, VSD, AS, PDA, CGA, Blalock-Taussing shunts, Prosthetic valves (but it is very rare with ASD)
- Microbial invasion of heart valves or mural endocardium results in infective endocarditis (IE). It leads to destruction of underlying tissue (→ valve perforation, ring abscesses formation)
- **M/c organisms in Infective Endocarditis (IE)**
 1. Overall --- Viridans streptococci
 2. After dental / URT procedure --- Viridans streptococci subtypes **sauguis**
 3. I/v drug abuser --- S. aureus (Rt.sided) --- Enterococci (Lt.sided)
 4. Native valve IE (Community acquired) --- Viridans streptococci
 5. Native valve (health care associated/ nosocomial) --- Staph. aureus
 6. Prosthetic valve IE --- Coagulase -ve staph (epidermidis/albus) --- Viridans strepto (>12 months)
- Best time for taking culture is - after 2-3 days of onset of symptoms just before starting antibiotics.
- Roth's spots are seen in acute BE.
- Hemotoxylin bodies of Gross are seen in Libman Sach endocarditis in SLE
- Mitral valve is the m/c valve involved in RHD, IE, valve prolapse, NBTE.
- Valvular abnormalities seen in carcinoid heart disease are → TR + PS (secondary to fibrogenic effect of serotonin).
- The hallmark of IE is presence of friable, bulky, potential destructive vegetations containing fibrin, inflammatory cells & bacteria/ other organisms.
- **M/c lesion of rheumatic mural endocarditis is Mac Callum's patch**, found in → Posterior wall of left atrium.
- Soldier's spots or Milk spots (pericardial fibrous plaques) are seen in → Anterior surface of right ventricle in healed or chronic pericarditis.
- Myxoma is m/c situated in → left atrium. (Myxoma is the m/c cardiac tumour in adults).

Embolic c/c in IE

- Rt sided lesion → involve lungs
- Lt sided lesion → involve brain, spleen, kidney, etc. (but not lungs)

ENDOCARDITIS : Location of Vegetations

	Rheumatic	Libman Sacks	NBTE (Marantic)	Bacterial
Seen in	RHD	SLE, TTP	Cancer patients	Infective
M/c valve involved	Mitral (sometimes aortic)	Mitral, tricuspid	Mitral (less often aortic, tricuspid)	Mitral, aortic
Micro	Aschoff's bodies ⁺	Hematoxylin bodies of Gross		Valve perfora ⁿ & ring abscesses are seen along the line of closure
Location of vegetation	Along the line of closure	Valve pockets/ undersurface of valve Both surface (atrial + ventricular) of valve leaflets + pockets (undersurface of valve)	Along the line of closure	<u>SABE</u> - on previously diseased valve <u>ABE</u> - on previously normal valve
Vegetations are	Small, multiple, warty & firm (No embolic phenomena)	Flat, spreads over mitral valve & chordae m/s (No embolic phenomena)		Large & friable (Thromboembolism is most common)

- M/c cause of infective endocarditis in India --- RHD
- Endocarditis occurring among IV drug abusers usually involves tricuspid valve and caused by *S. aureus*.
- M/c valvular disease a/w IE --- MVP with regurgitation.
- M/c valve involved in IE --- mitral valve.
- M/c cardiogenic source of systemic embolization is --- Mural thrombi
- Paradoxical emboli are seen in --- ASD
- Ring abscess are --- Vegetations involving myocardium in IE
- Microabscesses in brain & meninges occur commonly in *S. aureus* endocarditis.
- Mycotic aneurysm are --- Septic/bacterial in origin

- o **Mycotic aneurysms**--- Are focal dilatations of arteries occurring at points in the artery wall that have been weakened by infection in vasa vasorum or where septic emboli have lodged

PERICARDITIS

- o M/c type --- Serofibrinous / fibrinous (It is a bread and butter type of pericarditis seen in rheumatic carditis)
- o M/c cause of chronic pericarditis → TB
- o M/c collagen vascular disease a/w P~ → SLE (pericarditis is the m/c cardiac manifestation of SLE).
- o M/c cause of constrictive pericarditis → TB
- o M/c cardiac manifestation of rheumatic carditis → Pancarditis
- o Fibrous pericarditis is seen in → TB

GIT & LIVER

Mucosal Changes in Malabsorption

Mucosal changes	Conditions
1. Total villous atrophy	- Coeliac ds.
2. Partial villous atrophy	- Food protein sensitivite enteropathy, Giardiasis
3. Specific lesions on intestinal biopsy	
o Fat filled enterocytes	- Abetalipoproteinemia
o Villi distorted by ectatic lymphatics	- Lymphangiectasias
o Presence of PAS +ve macrophages containing the characteristic small bacilli	- Whipple's disease

S.I. Biopsy has diagnostic value in :

- o Whipple's disease (sub total villous atrophy)
- o Abetalipoproteinemia (villi - normal)
- o Agammaglobulenemia (Flat or -nt villi)
- o MAI - complex

Biopsy is Abnormal but not diagnostic :

- Celiac sprue (short / -nt villi)
- Tropical sprue, Collagenous sprue
- Acute radiation enteritis
- Folate / B₁₂ deficiency

Comparison b/w Whipple's disease, Coeliac Sprue & Tropical Sprue:

	Whipple's disease	Coeliac sprue	Tropical sprue
Also k/as	-	Gluten sensitive enteropathy Non-tropical sprue	Tropical Jejunitis
Etio	Tropheryma whipellii	Gluten containing diet (Barley, Rye, Oat, Wheat Mnemonic : BROW)	Iron, B ₁₂ , Folate deficiency d/to jejunitis
HLA	-	HLA DQ2	-
Patho	Subtotal villous atrophy	Villous atrophy + crypt hyperplasia	Mononuclear infiltration in jejunum/ distal ileum
Biopsy	Diagnostic	abnormal	abnormal
Cl/F	Abdominal pain, arthralgia, seteatorrhoea, fever (Systemic features)	-	-
Lab/F	Lymphogranuloma ↓ Xylose absorption	↑ IgA, ↑ tTG, anti-sacharomyces cervicase antibody	Megaloblastic anemia
T/t	Co-trimoxazole	Gucocorticoids, avoid gluten containing diet	Tetracycline, sulfonamide, B ₁₂ & Folates

- The presence of *T. whipple* bacillus outside of macrophages is a more imp. indicator of active disease than their presence within the macrophages
- Infectious etiology is seen in Whipple's disease & Tropical sprue, so both are treated with antibiotics.
- Systemic features are present in Whipple disease.
- Immune etiology is seen in Coeliac sprue so immuno suppressant (steroid) are nseful in it.
- Jejunal lactase deficiency leads to diarrhea with the ingestion of milk
- D-xylose test is best in assesment of absorptive function of intestinal mucosa
- NBT-PABA test is widely used test to assess pancreatic exocrine insufficiency

Non Cirrhotic Portal Fibrosis (NCPF)

- NCPF is a vascular disorder of liver characterized by fibrous thickening of portal vein or its branches.
- Hallmark of the d/s is thrombosis / sclerosis of the portal vein branches. Vessels are formed often termed as mesangiosinoids or periportal cavernoma.
- Portal and periportal fibrosis.

- **Bile-infarcts** --- Seen in 2° biliary cirrhosis (SBC)

Bile - plugs --- Seen in intrahepatic cholestasis

Bile - lakes --- Seen in extrahepatic cholestasis & SBC

- *Infarcts of Zahn* are seen in liver d/to occlusion of intra-hepatic branch of portal vein. Necrosis is not seen. There is marked stasis in distended sinusoids with secondary hepatocellular atrophy.

Liver Cell Necrosis

Type	Subtype	Seen in
Diffuse/ Massive	>2	◦ Viral hepatitis
		◦ Typhoid
		◦ Brucellosis
		◦ Tularemia
		◦ Herpes
		◦ Adeno virus
Zonal	Centrilobular (Zone 3)	◦ Shock, CHF
		◦ Ischemic Injury
		◦ CCl ₄ , chloroform, halothane
		◦ CVC Liver
	Midzonal (Zone 2)	◦ Yellow fever
		◦ Viral Hepatitis
	Periportal (Zone 1)	◦ Phosphorus
		◦ Pre-eclampsia
		◦ PEM
		◦ Alcohol (3P ⁺ + A)
Focal		◦ Miliary TB
		◦ Typhoid
		◦ Drugs
		◦ Viral hepatitis

- Nodular regenerative hyperplasia of liver is seen in --- Alcoholic hepatitis.
- Periportal fibrosis is a/w --- Alcoholic liver injury.

STEATOSIS

(Fatty changes/Fatty Degeneration of liver)

Steatosis (Fatty change)	Feature	Seen in
o Macrovesicular	Macrovesicular is more common	Alcoholism, Obesity, Obstructive sleep apnea, Insulin resistance
o Microvesicular	Small intracytoplasmic fat vacuoles (Liposomes) accumulate	Reye's syndrome, Tetracyclines, Valproate, CCL ₄ , Acute fatty liver of pregnancy, Hepatitis D.

- o Abnormal retention of lipid (TG) within a cell. Excess lipid accumulates in vesicles that displace the cytoplasm.
- o When the vesicles are large enough to distort the nucleus, the condition is k/as macrovesicular steatosis; & if small, the condition is k/as microvesicular steatosis.
- o *Alcoholism (Alcoholic Fatty Liver d/s, AFD):*
 - Alcoholism (overdose of ethanol) is the m/c cause of fatty liver.
 - The breakdown of large amounts of ethanol in alcoholic drinks produces large amounts of chemical energy, in the form of NADH, signalling to the cell to inhibit the lipolysis.
 - Alcohol causes periportal necrosis → periportal fibrosis
 - *Maddrey's index* is used for alcoholic hepatitis include PT, control PT, T. bilirubin. If it is >32 indicates poor prognosis.
 - Alcoholic hepatitis causes all three i.e. Mallory Hyaline, Fatty changes and ballooning degeneration
- o *NAFLD (Non- Alcoholic Fatty Liver d/s):*
 - M/c cause of chronic liver d/s in US.
 - Include steatosis, NASH (Non-alcoholic steatohepatitis)
 - The oxidative stress acts upon accumulated lipids → Lipid peroxidation.
- o Longstanding AFD, NAFLD, NASH leads to → cirrhosis.
- o Overdose of tylenol (paracetamol) is the m/c cause of acute liver failure.

CIRRHOSIS OF LIVER : Types

Micronodular	Macronodular	Mixed nodular
ICC	Post-necrotic	Alcoholism
Secondary biliary cirrhosis	Wilson's d/s	Tyrosinemia
Hemochromatosis		
Portal/Nutritional/Laennec's cirrhosis (In Alcoholism, Malnutrition, severe anemia)	<i>Risk of hepatic malignancy is more with macro-nodules.</i>	α-1 Antitrypsin deficiency

Causes of

- Mallory Hyaline**
- o Alcoholic hepatitis/ cirrhosis
 - o Focal Nodular Liver hyperplasia
 - o PBC
 - o ICC
 - o HCC
 - o Wilson's disease
 - o Chronic cholestasis syndrome

- Fatty changes**
- o α₁AT def.
 - o Rye's syndrome
 - o Starvation, Malnutrition
 - o Obesity, DM
 - o Alcoholism
 - o Late pregnancy
 - o Valproate T/t (but NOT in ICC)

- Ballooning degeneration**
- o Acute viral hepatitis
 - o Alcoholic Hepatitis
 - o Drug induced

- Piecemeal (troxis) necrosis**
- o Chronic viral hepatitis
 - o α₁AT def.
 - o Autoimmune hepatitis
 - o Steohepatitis, PBC

→ Jaundice is usually not seen in ---- Rye's syndrome.

→ Mallory Hyaline is not seen in ----Congenital hepatic fibrosis

→ Fatty changes are not seen (or rare) in ---- ICC.

→ Poisoning that leads to yellow fatty liver --- Arsenic

KIDNEY & GUT

Glomerulonephritis

	Examples	Remark
Nephrotic syndrome	Membranous nephropathy	M/c cause of NS in adults
	MCD (Minimal change d/s)	M/c cause of NS in children
	FSGS	
Nephritic Syndrome	ADP GN (post streptococcal GN)	
	Ig A nephropathy	M/c cause of nephritic syndrome worldwide
	RPGN	
	MPGN type I and II	

NEPHROTIC SYNDROME

- M/c cause in children— minimal change nephropathy
- D/g
 - Triad of proteinuria ($>3.5\text{g}/1.73\text{ m}^2\text{ BSA}$) + Hypoalbuminemia + Hyperlipidemia and edema
 - massive edema (m/c sign)
 - massive proteinuria ($>2\text{g/d}$), selective hypoalbuminemia ($<2.5\text{ g/dL}$)
 - hypercholesterolemia ($>200\text{ mg\%}$) esp $\uparrow\uparrow$ LDL and VLDL.
 - Absence of nephritic features like oliguria / hematuria / hypertension
- AR & AD forms of Steroid resistant NS (FSGS) have been described.
- Gene mutation a/w congenital NS (Finnish type) --- Nephrin (NPHS 1 gene product)
- Gene mutation a/w steroid resistant NS (FSGS) --- Podocin (NPHS 2 gene product)
- Screen the child for TB & HBs Ag before starting t/t
- MCNS shows normal histology on light microscopy
- Thrombotic and thromboembolic c/c are due in part to loss of endogenous anticoagulant (AT-III) and antiplasmins or plasmin inhibitors in urine.

Genetic basis of proteinuria in NS

- NPHS 1 gene maps for chromosome 19q13. It encodes protein nephrin. Mutations in NPHS1 gene result in congenital (finnish type) NS. MCD like glomerulopathy.
- NPHS 2 gene maps to chromosome 1q25-31. It encodes protein podocin. Mutations in NPHS2 gene result in idiopathic steroid resistant NS of childhood.
- α actinin 4 gene encodes podocyte actin binding protein. Mutations in α actinin 4 gene result in autosomal dominant FSGS.
- TRPC 6 gene mutation \uparrow Ca influx in podocytes and result in adult onset FSGS.

NEPHRITIC SYNDROME

- Acute N~ is also k/as poststreptococcal GN
- There is recent h/o streptococcal impetigo. Nephrogenic strains of streptococci are serotype 49 (pyoderma) and serotype 12 (pharyngitis)
- Triad of oliguria + hematuria + edema with or without uremia, ARF, and hypertension
- Confirmed by +ve ASO titre, anti- DNAase, streptokinase, hyaluronidase/ streptozyme tests. ASO titre may not be +ve following skin infection d/to trapping of antigens in subcutaneous fat, in such case DNAase is +ve.
- Prognosis is good & recovery is complete in ~ 95% cases
- Renal vein thrombosis (RVT) in nephritic syndrome is d/ to loss of anti-thrombin III.
- Complement C3 levels will be low in post infective GN, MCNS and SLE (lupus nephritis), but will be normal in Ig A nephropathy and Good Pasture d/s
- Renal parenchymal d/s constitute 78% of all (of which chronic glomerulonephritis is the m/c cause) cases of hypertension in children.

Imp. causes of hematuria

Streptococcal/

Post-infective GN	---	C3 low
IgA nephropathy	---	C3 normal
RPGN	---	fatal progression
SLE	---	ANA, ds DNA +ve . C3 low
Nephritic onset		
nephrotic syndrome	---	Massive proteinuria, high s. cholesterol
Alport	---	familial, deafness, lens dislocat ⁿ

HUS --- Bleeding, hemolytic anemia, thrombocytopenia

- Urine analysis in a patient with hematuria and hypercalciuria is most likely to reveal eumorphic RBCs (isomorphic RBCs).

- Glomerulo nephritis with normal complement level :*

- Immune complex mediated GN, IgA nephropathy / HSP
- RPGN (Crescentic GN)
- ANCA associated pauci-immune GN (WG, PAN) & Anti-GBM disease (Good Pasture's syndrome)

- Low complement levels (Hypocomplementemia) :*

- MPGN (type -II)
- PSGN (Post streptococcal)
- SLE nephritis
- Chronic infections

- Factors predisposing to thrombosis in NS (Nephrotic syndrome) :-*

- Hemoconcentration from hypovolemia
- Increase blood viscosity, raised Hct.
- Hyperfibrinogenemia, Raised lipoproteins
- ↓AT-III and protein S.
- ↓serum transferrin, hypocalcemia, ↓TBG,
- ↓ceruloplasmin

- GN with initial steroid resistance is seen in :*

- FSGS
- Membranous nephropathy, Membranoproliferative GN, Mesangioproliferative GN

- Enlarged kidney is seen in:*

Polycystic kidney disease (PKD)
Hydronephrosis
Amyloidosis, DM

- Small Contracted Kidney is seen in :*

1. Chronic GN (granular scars) - B/L
2. Chronic Pyelonephritis (U-shaped scar) U/L
3. Benign nephrosclerosis (V-shaped scar) B/L,
4. Amyloidosis, Myeloma kidney,
5. Diabetes mellitus B/L contracted but not granular

- Flea-bitten Kidney is seen in :*

Acute post streptococcal GN (ADP-GN),
RPGN,
HUS, TTP,
HSP, PAN, Infective Endocarditis,
Malignant nephrosclerosis (Hypertension).

Glomerular manifestation of protozoan and parasitic infections

Organism	Renal manifestation
Plasmodium falciparum	Transient proteinuria (50%), NS d/to MPGN (<1%)
P. malariae	NS
Toxoplasma	Mesangial GN
Filariasis	MGN
Schistosomiasis	NS, ESRD

- Collapsing glomerulopathy (a variant of FSGS) is seen in HIV

- P. malariae is a/w --- MGN (membranous GN)

- M/c GN in Leprosy --- MPGN (membrano-proliferative)

- M/c GN in IgA nephropathy --- Mesangio proliferative GN

- S. aureus is the m/c organism causing shunt nephritis in children

- In RPGN kidneys are enlarged and pale. Often petechial hemorrhages are present on cortical surface (flea beaten appearance)

- MPGN type-II is a/w partial lipodystrophy, positive C3 NeF (nephritic factor) & hypocomplementemia

- MPGN Type-II has a high rate of recurrence in the transplanted kidney

- Though MGN is rare in children, hepatitis B is the most frequent cause of MGN (membranous nephropathy) in children. Anti-e antibodies are seen with spontaneous remission.

- Both nephrotic and nephritic syndromes are seen in MPGN.

- Renal vein thrombosis is a/w membranous nephropathy

- Renal vein thrombosis in nephritic syndrome is d/to --- Loss of anti-thrombin III

- Hyalinosis is a common feature of focal segmental glomerulosclerosis

- Cells commonly seen in a patient with renal disease ---- Burr cells.

Glomerulonephritis	Cl/F	Etiology
<ul style="list-style-type: none"> ADP - GN Diffuse proliferative GN Acute - GN 	<ul style="list-style-type: none"> Nephritic syndrome Gross hematuria + edema + HTN Oliguria ↓ complement C3 RBC casts: <i>most specific</i> 	<ul style="list-style-type: none"> Leprosy, ABE, SABE Post-streptococcal ($2/3$rd cases)
<ul style="list-style-type: none"> RPGN (Crescentic GN) 	<ul style="list-style-type: none"> Sub acute RF Nephritic synd Complement level Normal (post streptococcal 5%) Respiratory symptoms⁺ (hemoptysis⁺ in GPS) 	<p>RPGN TYPE</p> <ul style="list-style-type: none"> I- Idiopathic, Good pasture synd II- Idiopathic, SLE, post infectious III- WG, PAN Churg-Strauss synd
<ul style="list-style-type: none"> Minimal change disease (MCD) (Lipoid nephrosis/ Nil deposit d/s) 	<ul style="list-style-type: none"> Most common cause of Nephrotic syndrome in children Lipiduria & Lipid cast in urine Good response to steroids 	<ul style="list-style-type: none"> Idiopathic is the m/c cause drugs (Rmp, NSAIDS, Iron-dextran, IFN-α) HIV HD, Allergy, interstitial nephritis
<ul style="list-style-type: none"> Membranous GN (MGN) (Haymms GN) 	<ul style="list-style-type: none"> Most common cause of Nephrotic syndrome in <u>adults</u> 	<ul style="list-style-type: none"> Idiopathic (in primary) SLE & Infections (HBV, HCV, Syphilis, P. malariae) Drugs (penicillamine/ Gold, Captopril, NSAIDS)
<ul style="list-style-type: none"> Membranoproliferative GN (MPGN) Mesangiocapillary GN 	<ul style="list-style-type: none"> Nephrotic (type - I) Type-II is a/w partial <u>lipodystrophy</u> Hypocomplementemia 	<ul style="list-style-type: none"> MPGN type-I (H/O recent URI) MPGN type-II (<i>Dense deposit ds</i>) MPGN type-III
<ul style="list-style-type: none"> Focal GN (FGN) focal proliferative GN focal segmental GN 	<ul style="list-style-type: none"> Variable Hematuria 	<ul style="list-style-type: none"> Idiopathic (Primary) Secondary in -SLE, HSP, WG, SABE IgA nephropathy, DM
<ul style="list-style-type: none"> Focal segmental glomerulosclerosis (FSGS) (collapsing glomerulopathy) 	<ul style="list-style-type: none"> Nephritic >80% microscopic hematuria Hypertension Steroid <u>resistant</u> 	<ul style="list-style-type: none"> Primary-idiopathic Secondary to HIV, Heroin, CMT syndrome, lysosomal ds, morbid obesity, <u>minimal change ds</u>, <u>Chronic pyelo nephritis</u>, reflux uropathy/ nephropathy
<ul style="list-style-type: none"> IgA nephropathy (Berger's disease) 	<ul style="list-style-type: none"> Asymptomatic gross/microscopic recurrent hematuria Most common cause of <u>nephritic synd.</u> worldwide 	<ul style="list-style-type: none"> Mucosal infection - URI-viral (>50%) Flu-like syndrome

Pathogenesis	Pathology : LM	EM	IFM [Granular IgG + C ₃]
<ul style="list-style-type: none"> Immune complex (local/circulating) trapping 	<ul style="list-style-type: none"> Diffuse proliferation <i>Endocapillary proliferation</i> 	<ul style="list-style-type: none"> Subepithelial deposits (Humps) <i>Lumpy bumpy deposits</i> 	<ul style="list-style-type: none"> + (Irregular)
<ul style="list-style-type: none"> Anti-GBM antibodies 	<ul style="list-style-type: none"> <i>Crescents</i> (parietal epithelial cells + mesangial cells + macrophage) <i>Rupture of GBM</i> 	<ul style="list-style-type: none"> No deposit Sub epithelial No deposit 	<ul style="list-style-type: none"> + but <u>Linear</u> COL₄ A₃, Anti-GBM Ab in Good P.S.
<ul style="list-style-type: none"> Immune complex Pauci-immune 			<ul style="list-style-type: none"> + (But C-ANCA +ve >90%)
<ul style="list-style-type: none"> -ve charge on GBM CMI? 	<ul style="list-style-type: none"> Normal 	<ul style="list-style-type: none"> <i>Loss of foot processes</i> 	-
<ul style="list-style-type: none"> Immune-complex (Local) 	<ul style="list-style-type: none"> Diffuse <u>thickening</u> of GBM 	<ul style="list-style-type: none"> <u>Sub-epithelial spikes & dome pattern</u> 	<ul style="list-style-type: none"> + (C_{5b-9} terminal components of complement also +nt)
<ul style="list-style-type: none"> I- Imm-complex (70%) II- Alternate pathway activation III- Systemic ds 	<ul style="list-style-type: none"> <u>Split / double counter tram track GBM</u> Membranous thickening Epimembranous deposition 	<ul style="list-style-type: none"> I- <u>Sub-endothelial</u> II- <u>Dense intramembranous</u> III- Sub-endo-/epithelial 	<ul style="list-style-type: none"> + (also C₁ & C₄) + <u>properdin, NeF</u> + (also C₃, IgM)
<ul style="list-style-type: none"> Immune-complex 	<ul style="list-style-type: none"> Segmental area of proliferation of cells & necrosis sometimes crescent 	<ul style="list-style-type: none"> Mesangial deposits 	<ul style="list-style-type: none"> + (also IgA, <u>fibrin</u>)
<ul style="list-style-type: none"> No cellular proliferation Hyperfiltration injury 	<ul style="list-style-type: none"> Focal & segmental sclerosis & hyalinosis (Tuft necrosis) 	<ul style="list-style-type: none"> <i>Loss of foot processes</i> Electron-dense deposits in sclerotic / hyalinosis region 	<ul style="list-style-type: none"> - (but IgM, C₃ present)
<ul style="list-style-type: none"> Alternate pathway disease? 	<ul style="list-style-type: none"> FGN (<u>mesangio-proliferative glomerulonephritis</u>) 	<ul style="list-style-type: none"> Electron-dense <u>mesangial deposits</u> 	<ul style="list-style-type: none"> + (also IgA, C₃ properdin)

Kidney in Hypertension (Nephrosclerosis)

	Benign hypertension	Malignant hypertension
1. Renal change	Benign nephrosclerosis	Malignant nephrosclerosis
2. Gross	↓ in size, surface is granular (grain leather appearance)	↓ in size, Cortical surface showing pinpoint petechial hemorrhages (<i>Flea bitten kidneys</i> + contracted /normal kidneys)
3. Histo-patho	Hyaline arteriosclerosis, Fibroelastic hyperplasia	Hyperplastic arteriosclerosis, Fibrinoid necrosis, Concentric laminar thickening → Onion skin app.

Acute Tubular Necrosis

○ Toxic :

Nephrotoxic poisons causing necrosis of PCT are

Cd, Hg (mercury), phenol, CCl₄. Acute liver failure is a/w toxic ATN.

○ Ischemic:

Patchy involvement, straight segment of PT (= PST), ascending limb of HL are most vulnerable.

RENAL PAPILLARY NECROSIS

- A descriptive term for a condition, necrosis of the renal papillae, that has various possible causes. The renal medulla and papillae are vulnerable to ischemic necrosis.
- Causes are : [POSTCARDS]
Pyelonephritis, UTI
Obstructive uropathies,
Sickle cell disease,
Tuberculosis,
Chronic liver disease,
Analgesics /alcohol abuse,
Renal transplant rejection,
Diabetes mellitus,
Systemic vasculitis (SLE).
- **Analgesic nephropathy is the m/c cause of renal papillary necrosis.** The damage is cumulative. The risk is higher for phenacetin and acetaminophen (paracetamol) compared to aspirin and other NSAIDs.

Medullary sponge Kidney

- Benign condition a/w medullary cysts are seen on excretory

urography a/w calcifications

- Clinical features or complications are :
Renal stones, recurrent hematuria, infections (UTI)
- No inheritance.
- Renal functions are normal & no cortical scarring.

Nephrocalcinosis

- Hypercalcemia a/w ↑↑ levels of 1,25,DHCC may be observed.
- Seen in sarcoidosis, hyperphosphatemia, RTA, Renal TB, Medullary sponge kidney, Vit. D intoxication, hyperparathyroidism, renal transplant rejection, Renal papillary necrosis.
- Nephrocalcinosis is also seen in granulomatous diseases and lymphomas in which activity of the enzyme 1- α -hydroxylase is induced by interferon γ and TNF- α .

Fibronectin nephropathy

- AD condition c/by glomerular enlargement with PAS+ mesangial deposits.
- Non -amyloid (congo red -ve) and non-Ig derived organized deposits are seen.
- Ultrastructural findings are : Large mesangial and subendothelial deposits.
- Clf:proteinuria + slowly progressive renal deterioration.

POINTS OF SPECIAL MENTION

- In sarcoidosis there are 3 important cytoplasmic inclusions - Asteroid bodies, Schaumann's bodies or chonchoid bodies and Birefringent cytoplasmic crystals.
- In bronchial asthma microscopic diagnosis is based on - Curschmann's spiral, Charcot Layden crystals.
- In sarcoidosis - non cascating epithelioid cell granuloma (Kveim's test +ve)
In TB - Caseating granuloma (Mantoux +ve) but Kveim -ve
In Crohn's disease - Non-caseating granuloma
- Centriacinar (centrilobular) emphysema - In smokers, co-exists with chronic bronchitis, CWP [involves upper lobes of lung]
Panacinar emphysema - associated with α 1 - AT deficiency [involves lower zone]
Irregular (Para-cicatricial) emphysema - Most common form of emphysema, seen around scars from any cause
- Osler's nodes - In SABE, there are tender, painful erythematous nodules over finger tips hand/feet.
Janway's lesion - In ABE, painless, non-tender subcutaneous

maculopapular lesions over pulp of fingers.

- Thrombosthenin ----- is a contractile protein, produced by platelets.
- Thromboplastin ----- is a lipoprotein, clotting factor 3.
- **Thrombomodulin** ----- is a thrombin-binding protein produced by all endothelial cells except those in the cerebral microcirculation. Cell surface protein that binds thrombin, activate protein C & inhibits coagulation
- Thrombospondin ----- is present in bone.
- Thrombopoietin ----- is circulating protein factor, produced by liver and kidney, stimulates platelets.
- **Nephritic factor** is - IgG seen in type-II MPGN (C₃, properdin). C₃ Nephritic factor (C₃ NeF) is an antibody to the complement system comprising mostly of IgG immunoglobulins role in pathogenesis type-II MPGN causes hypocomplementemia.
- **Rheumatoid factor** is - IgM antibody directed against IgG
- **M-components** - IgG in 53% patients and IgA in 25% patients
- **Paraproteins** - In multiple myeloma there is increase synthesis. P~ are abnormal immunoglobulins circulating in plasma and excreted in urine. Most common para protein is IgG (in 2/3 cases of MM), IgA (M component is also a paraprotein)
- **Cryoglobulins** are - Proteins which are coagulated when plasma or serum is cooled / chilled to a very low temperature (2°C-4°C). Most commonly they are monoclonal IgG or IgM. (↑ in urine in RA, SLE, MM, Lymphocytic leukemia).
- **Bence Johns protein** are --- light chain proteins composed of κ & λ (Kappa and Lambda) mainly (in 80%) Their excretion in urine is increased in MM.
- **Tamm- Horsfall protein** - It is a urinary glycoprotein secreted by mucous glands of renal tubular cells in thick ascending limb of loop of Henle and distal tubule and may be seen as eosinophilic hyaline casts/pigmented casts in ischemic ATN. ◦ Paracortical LN hyperplasia is seen in **T-cells hyperplasia**, other conditions - phenytoin therapy, small pox vaccination, viral infections
- Necrotizing lymphadenitis on histopathology is seen in --- Kikuchi Fujimoto d/s
- Cavitory lesions are seen in --- Staphylococcus pneumoniae
- Microscopy in para ganglioma shows --- Dense core granules.
- Microscopy in PML shows--Inclusions in oligodendrocytes.
- Onion-bulb appearance on nerve biopsy in CIDP (chronic inflammatory demyelinating polyneuropathy) is d/to segmental demyelination and remyelination.

- **Mast cell d/s**: A/w irregular & patchy marrow infiltrates. Majority of mast cells are the fusiform type & contain variable no. of granules. Abundant no. of eosinophils & foci of reactive lymphocytosis are present. tryptase stains are strongly positive.
- Endotoxic shock is mediated by--- Endothelial injury.
- Oligoclonal bands are seen in --- Multiple sclerosis.
- Glowing of firefly is d/to --- ATP (luminescence substrate)
- **Assman's focus**--- The initial lesion in 2^o TB at the apex of the lung (infraclavicular) without any LN involvement is called Assman's focus. It begins as a small caseating tubercular granuloma.
- **Ghon's focus**--- The initial sub-pleural lesion in 1^o TB at the periphery of the lung.
- **Ghon's complex** --- Ghon's focus + draining lymphatics + enlarged peribronchial LN.
- **Cardiac polyp** --- Postmortem fibrinous clot in the heart

SOME IMP. NEGATIVE POINTS

- Gamma-Gandy bodies are NOT seen in PBS in ----- Thalassemia
- Spherocytosis in peripheral blood is NOT seen in ----- Thalassemia
- NOT an immune complex mediated disease ----- Good pasture syndrome.
- In PAN aneurysm are NOT seen at ----- extremities and pulmonary.
- Azurophilic or primary granules do NOT contain --- Collagenase.
- NOT a common cause of infective endocarditis ----- ASD
- NOT a complication of infective endocarditis ----- MI
- In Sickle cell anemia NOT seen ----- Leucopenia (in sickle cell anemia leucocytosis & thrombocytosis occurs)
- Iron def. anemia ----- is NOT a causes of sideroblastic anemia.
- Splenomegaly is NOT seen in ----- Tay Sach's, Sandhoff's disease.
- Fatty changes are NOT seen in ----- ICC
- RF is NOT +ve in ----- Typhoid (Enteric fever)
- Absolute lymphocytosis is NOT seen in ----- Enteric fever.
- Minimal change d/s is NOT seen in ----- Hepatitis B
- Focal GN is NOT seen in ----- HTN

- Nephrocalcinosis is NOT seen in ---- Polycystic disease or Multicystic Kidney disease.
- ATN is NOT caused by--- TB
- Bladder cancer is NOT caused by ---- TB
- In infective endocarditis thrombi are NOT found in---- Left atria
- Pale infarcts are NOT seen in---- Lung
- NOT seen in Rheumatic Aschoff's body ---- Epithelial cells.
- NOT a components of Dane particle ---- Delta antigen
- Mallory hyaline is NOT seen in ---- Acute viral hepatitis
- NOT seen in serum sickness ---- Anaphylaxis.
- Nephrocalcinosis is NOT seen in ---- polycystic kidney disease
- Low complement levels are NOT seen in ---- HUS
- Sterile vegetations are NOT seen in --- Infective endocarditis.
- Do NOT help in thrombus formation ----- Thrombomodulin
- **All endothelial cells produce thrombomodulin except----** endothelial cells of cerebral circulation
- NOT a/w hepatitis C ---- Scleroderma
- Hypersensitivity vasculitis is NOT seen in --- Veins
- NOT an example of granulomatous vasculitis ---- Buerger's d/s.
- NOT seen in xanthogranulomatous inflammation ---- presence of tuberculous infection.
- MHC-I is NOT found in --- RE cells.
- NOT a function of CD4 cells ---- Opsonization
- NOT a effect of bradykinin ---- Bronchodilatation.
- NOT a B-cell marker --- CD135
- NO role in opsonization --- CD4
- NOT a mediator of inflammation --- Myeloperoxidase
- NOT a channelopathy --- Tay-sach's disease
- Organ of the cadaver which can NOT be used for transplant --- Bladder
- NOT a bone marrow stem cell --- Myoblasts
- NOT a channelopathy ---- Tay-Sach's d/s
- NOT a predisposing factor for lymphoma --- Lynch syndrome

NOTES

PROTISTA

- Kingdom "Protista" include protozoan, algae, & fungus.

Prokaryotes vs Eukaryotes

Structure	Specification	Eukaryotes	Prokaryotes
1. Nuclear	Membrane	Well defined	absent
	All nuclear structures	+	-
		(DNA + Histone)	(Only DNA)
3. Cellwall	<u>Muramic acid</u> , <u>DAPA</u>	-	+
	Sterols	+	-
	Flagella	+	+
	Ribosome	80s (60s + 40s)	70s (50s + 30s)
4. Mitosis		+	-
5. Examples		Fungi, protozoa, slime moulds	Bacteria, Blue-green algae

- Eukaryotic cellwall (cell membrane) is made up of carbohydrate, lecithin, cholesterol but muramic acids, DAPA and triglycerides are -nt.
- Bacterial cellwall is made up of **peptidoglycan**.
- Fungal cellwall is made up of **chitin**.
- Eukaryotic ribosomes (fungi, protozoa) are 80s ribosomes (60s + 40s subunits).
- Prokaryotic ribosomes (bacteria) are 70s ribosomes (50s + 30s subunits).
- Plasmids are seen in prokaryotes.

Nosocomial Infection

- Also termed as *health care associated* infection.
- Acquired during the course of hospitalization.
- Most infections that become manifest after 48 hours are considered to be nosocomial. C/b manifest after discharge.
- Should not be present at the time of admission
- Source is exogenous (may be hospital ecosystem)
- They may be iatrogenic (induced during diagnostic/therapeutic intervention) or opportunistic.

In recent years gram positive cocci (*staph. aureus*) have become the most important group of hospital pathogens.

- *M/c type of N~ are UTI, usually a/w catheterization and urological procedures. (Klebsiella is the m/c pathogen involved)*
- *Staph. aureus is the commonest organism causing hospital acquired wound infections/ surgical wounds.*
- *Major organisms of concern in nosocomial pneumonia are gram-ve aerobic bacteria*

STERILIZATION

◦ Sterilization :

An article, surface or medium is made free of all living microorganisms including spores.

◦ Antiseptics :

When applied to living tissues (skin or mucosa) they prevent infection by **inhibiting** growth of bacteria.

◦ Disinfection:

When applied to non-living tissues disinfectants kills all pathogenic organisms but not spores. Heat is a disinfectant but not an antiseptic.

◦ Irradiational sterilization :

Ionizing radiations such as X-rays, **gamma rays** and cosmic rays sterilize without ↑ in temperature and thus this method is *k/* as cold sterilization.

Non-ionizing radiations such as IR -rays and UV rays are used for labs, OT, and inoculation hoods.

Hot air oven

- Utilizes 180°C × 1 hour
- Used for **lab glasswares** / glass syringes, petri dishes, test tubes, flasks, surgical instruments.
- Dusting powder, oils / greases, liquid paraffin (vaseline)
- It may destroy plastic/ rubber objects (mattresses) & hot air has no penetrating power, so not useful for these.

Burning (incineration)

- Infected material like soiled dressings, beddings, animal carcasses are reduced to ashes.

Red heat in bunsen flame

- Metallic inoculating wires, tips of forceps, and needles are held in flame till they become red hot.

Autoclaving

- Attain temp of 122°C under 15 lb/sq inch pressure.
- Most effective for killing spores.
- Used for :
 - Linen, bedsheets, dressings, gloves, glass syringes.
 - **OT appliances**, all suture materials *except catgut*
 - Most of the culture media (require autoclaving at 121°C for 15 min)
- *Not suitable* for plastics (plastic syringes), sharp instrument (sharpness destroyed), catgut
- Spores of *Bacillus stearothermophilus* are used as sterilization control.

Inspissator

- 80°-85° C for ½ hr. (solidification)
- Used for media containing egg or serum

Tyndallisation (Fractional/ Intermittent sterilization)

- Principle is 100° C for 20 min in 3 successive days.
- Used for culture media containing egg, sugars/ gelatin e.g. *LJ media*, *Loeffler's serum slope*
- Kills spores and bacteria.

Seitz filters (Filtira" by chamberland/ membrane filters)

- Used for sterilization of **vaccines**, ascitic fluid, sera, toxins, sugars, culture media and antibiotic sensitivity discs.

Vaccine bath /Water bath

- Bacterial vaccines are sterilized at 60°C × 1 hour.
- Serum, body fluids c/b sterilized at 56°C × 1 hour in a water bath on several successive days.

Glutaraldehyde (2% solution = cidex)

- Used for
 - Lenses of cystoscope/ endoscope (immersed for 30 min. before use).
 - Rubber/ plastic tubes, face masks, corrugated tubes (used for ICD, ETT)
- Sporicidal

Formaldehyde gas

- Fumigation of OT / labs / rooms/ woolen blankets, wool and hides.

Ethylene oxide (EtO)

- Used for
 - Heart lung machine.
 - Sutures, fabrics, **disposable syringes/needles**
 - Heat sensitive articles
- Explosive, so not suitable for fumigation of rooms.

Ionising radiation (Cold sterilization)

- **Gamma rays** are mainly used for commercial sterilization of disposable goods (disposable syringes), swabs, cannulas, catheters, culture plates.
- **CATGUTS**, bandages, artificial bone & tissue grafts.

Other methods

- **Iodine** : For **Lippes loop**, skin disinfection. A drop of tincture iodine may be added to a litre of drinking water for disinfection in an emergency.
- **5% cresol** : used for sharp instruments.
- **Pasteurization** : 63° C × 30 min (Holder's) or 72° C × 20 sec (Flash method) is used for sterilization of milk.
- **Bleaching powder, cresol, formalin** : c/b used for disinfection of faeces, vomitus, & sputum. Chlorhexidine is NOT used for sputum disinfection.
- All disposable & heat sensitive items like ETT, breathing circuits, face masks, reservoir bags, adaptors, airways etc. are best sterilized by ethylene oxide gas sterilization.
- Second choice for these items is chemical sterilization by Glutaraldehyde 2% (Cidex solution).
- For fiber-optic scopes/endoscopes 2% glutaraldehyde is preferred method of sterilization.
- Laryngoscopic blades, Magill forceps & stylets and spinal/ epidural sets for reuse can be autoclaved.

Boiling

- Vegetative bacteria are killed at 90-100°C but it is not recommended for sterilization of instruments of surgical procedures.
- Boiling for 5-10 min (rolling boil) will kill bacteria but will not kill spores or viruses. Spores are destroyed only at ≥ 100°C (as in autoclaving).

Sodium Hypochlorite

- Available Cl₂ is 80,000 - 180,000 ppm.
- 100-200ppm containing freshly prepared hypo solution is recommended for sterilizing **infant's feeding bottles.**
- Disinfectant in **HIV+** vc pt.

Chlorination

- Cl_2 kills pathogenic bacteria, trophozoites of amoeba & Giardia.
- It has no effect on ---
 1. Spores
 2. Certain viruses (e.g. polio, HAV) except in high doses
 3. Cysts of amoeba and Giardia
 So water filtration (Sand filters) & boiling are more effective than chemical t/t with chlorine
- Hepatitis A virus : Disinfectant is 2% glutaraldehyde or 23% HCl or NaOCl with excess free Cl_2 . 1mg/L of free residual chlorine (high dose) can cause destruction of HAV in 30 min at pH ≤ 8.5 .
- Spores of clostridium tetani can withstand boiling & chlorination but are destroyed by autoclaving.

Biological controls of different sterilization methods:

Disinfectant	Bacterium used	Sub species	Remark
1. Hot air oven	<i>Bacillus subtilis</i>	niger	—
2. Autoclave	<i>Bacillus stearothermophilus</i>	—	—
3. EtO, Dry heat	<i>Bacillus subtilis</i>	globigii	Red pigment variant
4. Ionising radia ⁿ	<i>Bacillus pumilus</i>	—	—
5. Filtration	<i>Serratia marcescens</i>	—	<i>Pseudomonas diminuta</i> also

- *Bacillus stearothermophilus* is a thermophile organism whose spores are extremely heat resistant. Its spore are used as the biological indicator for determining efficacy of moist heat sterilization/autoclaves (plasma sterilization control), saturated steam and automatic Steris sterilizers.
- *Bacillus subtilis* is the biological indicator for testing dry heat sterilizers, ethylene oxide sterilizers.
- *Bacillus subtilis* is used in Guthrie's test.
- Spores of non-toxicogenic strains of *Cl. tetani* are used to test efficiency of dry heat (flaming, incineration, hot air oven)
- *Cl. botulinum* spores are the most heat resistant organism and require $120^\circ\text{C} \times 4 \text{ min}$ or $100^\circ\text{C} \times 330 \text{ minutes}$ for their killing.
- *Coxiella burnetii* are relatively heat resistant and survives in the holder method of pasteurization of milk.
- *Proteus* strains are used as antigens for Weil-Felix reaction. (*P. vulgaris* for OX 19 and OX2 while *P. mirabilis* for OXX)
- Efficacy of Disinfection: In Riedel walker test phenol is taken as the standard and by measuring phenol coefficient of the disinfectant.

Disinfectant	Bacteria	Spores	Virus	Susceptibility to organic matter
1. Formaldehyde	+++	+++	+++	—
2. Glutaraldehyde	+++	+++	+++	—
3. Hypochlorite (Cl_2)	+	+/-	+++	+++
4. Phenol	++	—	+	+/-

- Prion organisms & spores are most resistant to sterilizaⁿ.
- Order of resistance to sterilization:
Prions organism > spores > mycobacterium > nonlipid or small viruses > fungi > vegetative bacteria > medium sized viruses.
- EtO (Ethylene oxide) can kill all viruses, bacteria, fungi, and spores.
- Na-hypochlorite (25% available Cl_2) is recommended for killing prions.
- Bladder wash is done by 0.1% KmnO_4 (Candy's lotion), solution of acetic acid and silver nitrate.
- Hand wash :- Chloroxylonol, chlorohibitane, salvon, spirit, iodophors, isopropyl alcohol.
- For cleaning infected wound - Iodophors, acriflavin, salvon, H_2O_2 are used
- Removal of slough from wound - EUSOL, H_2O_2 .

IMMUNOLOGY

ANTIBODIES

- All antibodies are immunoglobulins (Ig).
- All immunoglobulins are glycoproteins consisting of 2 light chain and 2 heavy chain. Immunoglobulin subtypes (i.e., G, M, A, D, E) are determined by the type of heavy chain present.
- Heavy chains are structurally and antigenically distinct for each class while L chains are similar (either κ or λ)
- Ag combining site is at amino terminus composed of both H & L chains.
- Light chain consists of 1 variable and 1 constant region while H chain has 1 variable and >3 constant regions. Variable regions are responsible for antigen binding and constant region are responsible for biologic function.
- Fab fragment consists of both H and L chain while Fc fragment has only H chain. J chains is for polymeric antibodies.

IMMUNOGLOBULINS (Ig)

	IgG	IgA	IgM	IgD	IgE
c Structure/size	Monomer, Smallest	Dimer	Pentamer (Largest Ig), K/a millionaire molecule	Monomer	Monomer
c Valency	2	4	10		
c Amount in serum	75% (Major Ig of serum) (among IgG 65% is IgG ₁ type)		Minute	Minute	Least
c Concentrated in		Body secretions (provides local / mucosal immunity)		Present on human B-lymphocytes	Sub-mucosa
c Half life	Longest t _{1/2}		Short lived, disappear early from blood		Shortest t _{1/2} (2-3d)
c Transplacental passage	+ (Only Ab which crosses placenta)	-	Synthesis start by fetus at 20 wks (before birth)	-	-
c Heat stability	+	+	+	+	- (Heat labile)
c Complement fixation	++ via classical pathway	+	+++ (strongest activator of classical pathway)	X	Does NOT fix complement
c Agglutination	viral agglutination, Toxin neutralization		Agglutinating/lytic Ab		
c Opsonization	Opsonizing Ab (+ direct)		+ indirect by producing C ₃ b (opsonin) (ie phagocytosis)		Mediates Immediate HS (TYPE-1 HS)
c Properties	Precipitating Ab	Local Ab, secretory Ab, mucosal Ab, present in Peyer's patches	Antigen receptors on B-cell +nt		Atopic or reaginic Ab
c Other effects	Produced in 2 ^o immune response	Prevents attachment of bacteria / viruses to mucous membranes	Indicates acute / recent infection. Produced in primary immune response to an antigen.		
	Heterocytotropic Ab detected by PC anaphylaxis	Def. of Ig A is often a/w with overproduction of Ig E Ab (so ↑ risk of anaphylaxis)	Presence is an indicator of cong. infection (eg. syphilis)		Homocytotropic, P-K reaction+
	Acts as blocking Ab during desensitization in T/t of atopy				Susceptible to mercaptoethanol
c Importance	↑ excretion in multiple myeloma (light chains)	↓ in - kwashiorkor, GIT/ resp. disease	↑ excretion in Waldenstrom macroglobulinemia		↑ in parasitic infections

- Isotype switching is a gene rearrangement process whereby the μ and δ C_H gene segments are spliced out and replaced with either γ ϵ or α C_H gene segments.
- Hypermutation is a process whereby a high rate of mutations occur in the variable segments of both the heavy chain (V_H) and the light chain (V_L). Somatic hypermutation is a molecular phenomena responsible in immunoglobulin genes for affinity mutation of Ab response.
 - If a child is suffering from recurrent infections caused by bacteria having polysaccharide capsule, assay of IgG2 will be helpful in evaluation.
 - IgG is most potent (+++) in opsonizing.
 - IgM is most potent (+++) in fixing complement.
 - IgA and IgM are present in milk.

Antigen- antibody reaction curve

- Prozone phenomena is d/to --- Antibody excess
- Equivalence zone is d/to --- Antigen- antibody complex precipitation
- Post-zone phenomena is d/to --- Antigen excess

→ Covalent interactions are NOT seen in antigen -antibody complex formation.

Haptens

Molecule that are able to react with preformed antibodies but are unable to stimulate their production directly.

Superantigen

Protein molecules that stimulate large number of T-cell without processing of the protein toxin by APCs (irrespective of their antigenic specificities).

- Staphylococcal enterotoxins (as in pathogenesis of *Kawasaki disease*)
- Toxic shock syndrome toxin (TSST-1).
- Group A streptococcal pyrogenic exotoxin A

These antigens directly bind to invariant region (lateral aspect of TCR β -chain) MHC antigens. They bind outside of MHC protein and T-cell receptor and are very active in low concentration.

Monoclonal antibodies

There are 3 major steps to produce monoclonal antibodies. These are --- fusion, selection, and screening.

- Methods of cell fusion to produce monoclonal antibodies are --- adding ethylene glycol, small electric current, and reducing the viscosity of membrane.
- B-cell hybridomas produces the same antibody as the parental B cell.
- **Trastuzumab (Herceptin)** is a humanized monoclonal antibody to HER2/neu developed to specifically target tumor cells and, it is hoped, spare normal cells. In clinical trials, the combination of Trastuzumab with chemotherapy improved response in patients with carcinomas overexpressing HER2/neu.

Antigens in Vaccinology

There are two types of antigens involved in production of antibodies / vaccines

- T cell dependent antigens (such as proteins and erythrocytes)
- T cell independent antigens (such as polysaccharides): They do not stimulate T-cells.

- *T - lymphocyte dependent vaccines*

Based on protein moieties, induce good immune responses even in young infants.

- *T - lymphocyte independent vaccines*

Polysaccharide /carbohydrate antigens based vaccines. Most IgG antibodies to polysaccharide antigens are IgG₂ type. There is B-cell response⁺ but no T-cell response. Poor immune responses in children <2 yr of age, immunity is short lasting/ short term & there is no enhanced or booster response on repeat exposure to antigen (i.e.lack of memory response).

Complements

- Complements are acute phase proteins.
- Liver synthesizes central components. Spleen, macrophages, and intestinal mucosa can also synthesize.
- Classical pathway is activated by --- IgM (most potent), IgG (requires 2 molecules), and immune complexes (eg. in SLE)
- In alternate C3 works on C3 convertase.
- C3 convertase splits C3 into → C_{3a} (Anaphylotoxin) + C3b (cell bound)
- Alternate pathway is activated by --- Bacterial *endotoxin* (most potent) and zymogen, IgA & IgG₄, cobra venom
- C3 is first common point b/w classical and alternate pathway. C3 is involved in both classical and alternate pathway.
- Functions : Basic functions of complements are opsonization, chemotaxis, lysis of foreign cells, and clumping of antigen bearing cells. Role in innate immune response.

Most important opsonizing complement (Major serum opsonin)	C3b
--	-----

Most important chemotactin	C5a
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Anaphylotoxin	C5a (most potent) C _{3a} , C _{4a}
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MAC (Membrane attack complex)	C5b - C9
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SRS-A (Slow reacting substances of anaphylaxis)	LT-C ₄ , D ₄ , E ₄
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Leukotriene which is chemotactic (Promotes leucocyte adhesion)	LT-B ₄
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↑Vascular permeability:	LTC ₄ , LTD ₄ , LTE ₄
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Vasodilatation	PGD ₂ , PGE ₂ , PGI ₂ , PGF _{2α}
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Complement deficiencies & their importance

Deficiency or ↓ level of	A/w
DAF	PNH
C1 esterase inhibitor	Hereditary angioneurotic edema
C2	M/c hereditary complement deficiency
C3	Alternate pathway activation
C3, C4	Classsical pathway activation
C1, C2, C4	SLE, Collagen vascular d/s
C6- C9	Nisseria

Serological Test

Principle	Type of test	Test
Agglutination	Tube	Widal test, Paul- Bunnel test for IM, Weil-felix reac ⁿ (Heterophile)
	Slide	Cold agglutinin, Blood grouping/cross match
	Latex slide	ASLO titre estimation, Cryptococcal Ag in CSF
	Passive slide hemagglutina ⁿ	Rose waaler test (for RA), Streptozyme test
Compliment fixation	CFT	Wassermann reac ⁿ for syphilis
Immuno florence	Direct	Rabies Ag detection
	Indirect	FTA-ABS in syphilis
Precipitation	Tube flocculation	Kahn's test for syphilis
	Slide flocculation	VDRL
	Ring precipitation test	Ascoli's thermoprecipitin test for anthrax, Lancefield test for streptococci

→ ASO titre is a neutralization test.

→ Shick test is for sensitivity & susceptibility to diphtheria. It is not a specific test.

CHEMOKINES

Chemokines receptors : CXCR4 are found mostly on T cells.,while CCR4 on macrophages. Anti HIV drug Maraviroc is an CCR5 antagonist.

Category	Type	Examples
C-X-C	α chemokines	IL-8
C-C	β chemokines	MCP-1, MIP-α, RANTES Eotaxin,
C	γ chemokines	Lymphotactin
CX3C	Fractalkine	

INTERLEUKINS

IL	Source	Function
IL-1	Macrophage	Pyrogenic, APR prolifera ⁿ & differentia ⁿ of T,B cells
IL-2	T _H 1	Activates B and T _H cells , cytotoxicity of T & NK cells
IL-3	T-cells	Stimulates hematopoiesis precursors/ pluripotent stem cell
IL-4	T _H 2	Proliferation of B-cell & T _C cells, ↑IgE
IL-5	T _H 2	B-cell differentiation, ↑IgA & IgM production, Eo differentiation
IL-6	T _H 1, macrophage	B-cell differentiation , ↑IgA production
IL-7	Spleen,BM, stromal cells	B & T cells growth factor
IL-8		Induces chemotactic response

→ IL-1, IL-6 & estrogens are involved in osteoporosis.

→ IL-12 is produced by macrophage & dendritic cells. It is critical for induction of T_H1 response.

→ IgG gives strong precipitation reaction and complement fixation test while IgM gives strong agglutination reaction.

→ Biological false positive reactions (BFP) are seen in -Leprosy(LL type), malaria, infectious mononucleosis, relapsing fever, hepatitis, collagen d/s, tropical eosinophilia

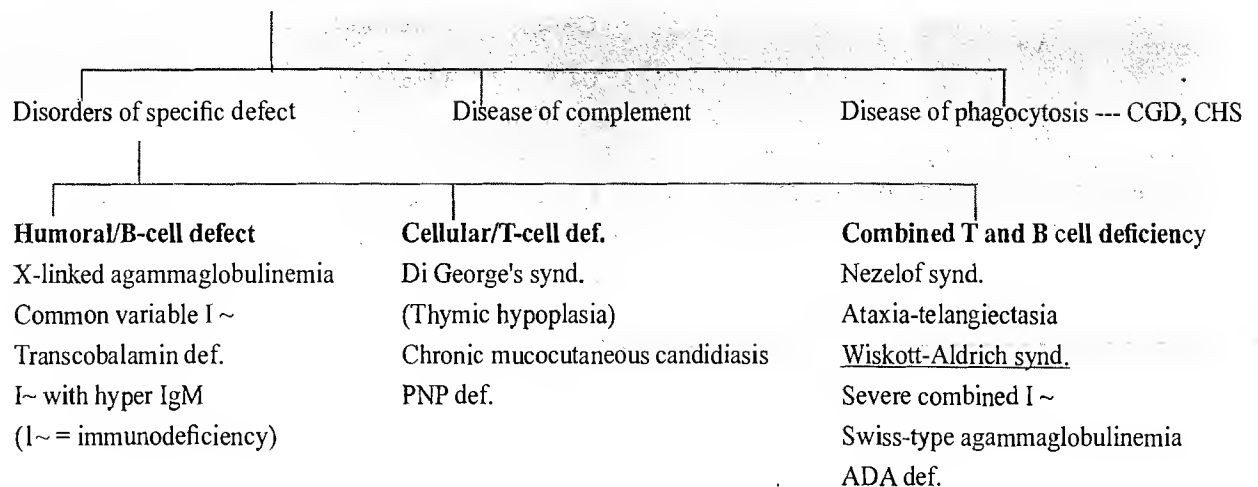
→ Anamnestic reaction is seen in persons who have had past typhoid/ enteric fever or who have had immunization against typhoid. They may develop A~ when they contract fever/ malaria.

→ Proinflammatory cytokines that are present with dominance of CMI---IL₂, INFγ, TNFα, IL₁

→ Anti-inflammatory cytokines that are present with dominance of humoral immunity----IL₄, IL₅, IL₆, IL₁₀

→ Most potent stimulator of Naive T-cells is --- mature dendritic cells

Important Primary immunodeficiency Syndromes



Bruton's agammaglobulinemia

X-linked d/s c/by **defective opsonization** d/to deficiency of opsonizing antibodies/immunoglobulins. Recurrent infections with encapsulated organisms are common. (CMI normal)

Common variable deficiency

Abnormal B-cell function, but serum level is normal. M/c associated with *giardiasis*. Deficiency of T-cell may be seen.

Ataxia telangiectasia

- o AR disorder c/by triad of cerebellar ataxia + oculocutaneous telangiectasia, and immunodeficiency.
- o ↓ IgE & absent IgA
- o A/w thymic hypoplasia, *recurrent sino - pulmonary infections*, premature aging, endocrine disorders (e.g. IDDM) high incidence of lymphomas, HD, leukemias (T-cells type)
- o Deficits in cerebellar functions --- nystagmus may be seen.

Chronic granulomatous disease of childhood [CGD]

- o Inheritance is XR or AR
- o D/to deficiency of **NADPH oxidase** leading to loss of peroxidase activity → inability to bleach (defective killing), even though the MPO are present in phagolysosomes
- o Screening test --- NBT test
- o Cause of death --- Sepsis d/to catalase +ve bacteria (commonly d/to staph. aureus)
- o Persistent CMI & humoral response

- o A/w seborrheic dermatitis, eosinophilia, granulomas of the intestine causing obstruction

Job's syndrome -

- o Hyperimmunoglobulin E.
- o Recurrent infections are common

Chediak - Higashi syndrome (CHS)

- o AR disorder a/w mutation in **LYST gene**
- o There is defective fusion of phagosome + lysosome [*giant lysosomes*] - giant primary granules are seen in neutrophils
- o D/to **defective phagocytosis** → abnormal killing
- o There is defect in microtubule polymerization & so leucocyte motility is impaired → **defective chemotaxis**
- o A/w
 1. Defect in platelet aggregation → Bleeding tendencies
 2. Defective nerve conduction in brain
 3. Oculocutaneous albinism as melanin synthesis require lysosomal enzyme.
 4. NK cell dysfunction, pancytopenia, photophobia & nystagmus
- o Leucocyte functions may be corrected by vit C 200mg daily.

Leucocyte adhesion deficiency (LAD)

- o Delayed umbilical cord separation.
- o CD 40 ligand deficiency.
- o Leucocytosis with few neutrophils. ↑ susceptibility to infection.

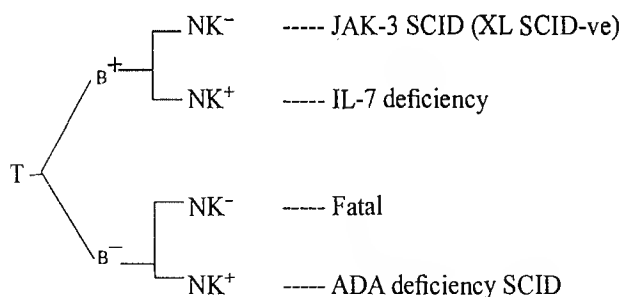
- Delayed fall/separation of umbilical cord is also seen in *alloimmune neutropenia*, *Sialyl Lewis X antigen deficiency*, *factor XIII deficiency*, *urachal anomalies*, and *histiocytosis-X*.

Wiskott Aldrich Syndrome

- XLR
- Eczema, bleeding tendencies (bloody diarrhoea in male newborn may be seen) d/to **thrombocytopenia**
- ↑ IgA & IgE but normal IgG, ↓ IgM, thymus normal.

SCID

- D/to lack of combined T,B,NK cells deficiency.
- X-linked form (SCIDX1) is a/w arrest of fetal thymus & lymphopenia, T- B+ NK-
- AR variants a/w ADA deficiency



→ NBT test is used to detect — defect in phagocytosis

→ Enzyme responsible for respiratory burst of phagocytic cells — NADPH Oxidase

Di-George Syndrome

- 3rd and 4th pharyngeal pouch syndrome.
- Results from failure of developmental of 3rd and 4th pharyngeal pouches.
- C/by hypoplasia /**absence of thymus** causing pure T-cell defect (**severest form of T-cell deficiency**) and severe defect in CMI.
- On CT scan there is no thymus and parathyroid glands are absent (resulting in **neonatal tetany**, hypocalcemia) aortic arch anomalies, deformed aortic knuckle, generalized osteoporosis. CATCH 22 spectrum results in d/to deletion of chromosome 22q.
- Condition is reversed by implantation of thymic tissue.

Nezelof's Syndrome

- Results from failure of development of **only 3rd** pharyngeal pouch.

- Superior parathyroid glands are present but inferior parathyroid glands and thymus are absent. So parathyroid functions are normal.

THYMUS

- *Thymic hypoplasia, aplasia or agenesis*

Is seen in **DiGeorge syndrome** and **Nezelof's syndrome**.

Patients have lymphopenia, ↓ immunity and they die from infections. Also seen in SCID (with reticular dysgenesis), and ataxia telangiectasia.

Acquired causes of thymic atrophy in young age are malnutrition, ionizing radiation, prolonged steroid/cytotoxic t/t.

- *Thymic hyperplasia*

B-cell follicles (germinal centres) are increased in number within the thymus. These patient develop Myasthenia gravis (MG) in 60-65% cases. It can also be seen in Grave's d/s, SLE, RA, scleroderma, cirrhosis.

- *Thymoma*

- M/c primary tumour of anterior mediastinum
- A/w MG, other autoimmune conditions and paraneoplastic syndrome such as acquired **hypogammaglobulinemia**, pure red cell aplasia, Grave's disease, PA, dermatomyositis, cushing syndrome.

→ Removal of thymoma (thymectomy), improves neuromuscular disorder (MG)

→ Thymic hyperplasia in a young female is a good prognostic predictor.

Prognosis after thymectomy is better if---

- Patient is young (< 40 year)
- Females benefit more
- Duration of d/s is shorter/ early stage of thymoma.
- Absence of thymoma
- A/w MG or thymic hyperplasia

BACTERIOLOGY

General Overview

- *Quellung's reaction* is swelling of bacterial capsule d/to increased refractivity. It is used to demonstrate antigenic nature of capsule. Also k/as **Neufold's reaction**. It was used for typing of pneumococci.
- *Nagler's reaction* is d/to α-toxin seen in *Cl. perfringens*.

- *Pfeiffer phenomenon* The alteration & complete disintegration of *V. cholerae* when introduced into the peritoneal cavity of an immunized Guinea pig.

M/c Organism Implicated in

- M/c species of pseudomonas causing intravenous catheter related infection — *Pseudomonas maltophilia*
- M/c organism implicated in osteomyelitis — *Staphylococcus aureus*
- M/c organism implicated in atypical pneumonia — *Mycoplasma*
- M/c cause of epidemic pleurodynia — Group B Coxsackie viruses, B3 and B5
- M/c cause of Handfoot mouth d/s — Coxsackie virus A16
- M/c viruses implicated in encephalitis — Echoviruses 9

Leptospirosis (Weil's disease)

- Caused by spirochaete *leptospira icterohemorrhagica*
- Characterized by triad of fever + jaundice (hemolytic) + renal failure (also k/as "icterohemorrhagic fever")
- Transmitted to humans by water contaminated with rat's urine. Farmer's are at increased risk.
- Rats are the most important reservoirs.
- D/g : Microscopic and macroscopic agglutination test (MAT)
- T/t : Tetracyclines or penicillins.

Lyme d/s (Borreliosis)

- Caused by *borrelia burgdorferi* causes.
- Incubation period is 3-30 days.
- Small red macule or papule is seen at the site of bite k/as erythema migrans.
- C/by triad of erythema migrans + facial nerve palsy + arthritis.
- FTA-ABS is positive but VDRL is negative.

Gas gangrene (Clostridial Myonecrosis)

- M/c caused by *clostridium perfringens* (cl. *Welchii*) type 'A' Its alpha toxin is a/w severity of ds. It can also be caused by other exotoxin producing clostridia viz. *clostridium septicum*, *cl. romnisum*, *Cl. novyii*, *cl. histolyticum*
- Strains are heat labile. Gas gangrene causing strains are destroyed within 5 minutes of boiling and food poisoning strains in 1-2 hrs.

Important tests

◦ Dick test, Schultz Charlton test	Scarlet fever
◦ Mc Fardye's reaction, Ascoli's thermoprecipitin test	Bacillus anthrax
◦ Diazo reaction, Widal test	Typhoid fever
◦ Rose Bengal test, milk ring test	Brucellosis
◦ Schick test, Elek's gel precipitation test	C. diphtheriae
◦ Eiken's precipitin test	ETEC
◦ Frei's test	LGV
◦ String test	Cholera
◦ Diene's phenomena	Proteus

Important Skin Tests are

- Lepromin - Leprosy
- Tuberculin - TB
- Frei - chlamydia (LGV)
- Kveim's - Sarcoidosis
- Fairley's - Schistosomiasis
- Casoni's : Hydatid disease

Intracellular Pathogens

- | | |
|--|--|
| ◦ <i>Listeria</i> (found in monocytes) | ◦ <i>Leishmania donovani</i> (neutrophils) |
| ◦ <i>Babesia</i> (RBC) | ◦ <i>Mycobacteria</i> (PMN). |
| ◦ <i>Plasmodia</i> (RBC) | ◦ <i>Histoplasma</i> (Macrophage) |
| ◦ <i>Trypanosoma</i> (Leucocytes) | ◦ <i>Gonococcus</i> (neutrophil) |
| ◦ <i>Salmonella</i> | ◦ <i>Cryptococcus</i> |
| ◦ <i>Toxoplasma</i> | ◦ <i>Microsporidia</i> |
- Obligate intra cellular organisms are - VCRL-MT Viruses, Chlamydia, Rickettsia, Legionella, *M. leprae*, *Treponema pallidum*

Bacterial oxygen requirement

- Obligate aerobes—*mycobacterium*, *pseudomonas*
- Microaerophilic—*Campylobacter*, *Helicobacter*
- Facultative—most bacteria
- Obligate anaerobes—*Actinomyces*, *Bacteroids*, *Clostridium* [ABC]

- *Pseudomonas* is an obligate aerobe but can grow anaerobically if nitrate is available
- *Vibrio cholerae* is strongly aerobic, growth is better in alkaline media

Transport Medias

- Pike's media --- Streptococcus pyogens
- VR media --- Vibrio
- Cary-Blair media --- Vibrio cholerae, shigella, salmonella, pasteurilla
- Stuart media --- N. gonococci
- Sach's media, SS media --- Shigella

Culture Media for Organisms

- Anthrax bacillus --- PLET medium
- Bordetella --- Bordet Gengou medium
- Brucella --- Castaneda method of blood culture
- Campylobacter jejuni --- Campy BAP, Skirrow's or Butler's media
- Chlamydia --- HeLa cells
- Clostridia (anaerobes) --- Robertson's cooked meat broth
- Corynebacterium diphtheriae --- Loeffler's serum slope, tellurite blood agar, Tinsdale media
- Listeria --- Blood agar, TSYE, ALOA, Oxford, Palcam
- Legionella --- BCYE medium
- Neisseria gonorrhoeae --- Thayer-Martin medium, Chacko nair, NYC medium, Chocolate agar
- Pseudomonas --- Cetrimide agar
- Shigella --- Deoxycholate Citrate agar (DCA)
- Spirochetes --- Noguchi's medium
- Staphylococcus --- Ludlum's medium
- Trypanosomes, leishmania --- Novy, McNeal, Nicole medium (NNN)
- To differentiate lactose and non lactose fermenters --- Mc Conkey's medium
- Pasturella/Yersinia --- Ghee broth
- Acanthamoeba --- E.coli enrichment on nutrient agar.
- Vibrio --- TCBS
- Salmonella --- Wilson-Blair
- E coli 0157 --- Sorbital, Mac Conkey media
- Mycobacterium TB --- LJ media

- Fungi --- Sabouraud's dextrose agar, Baker's media (for yeast)
- Proteus --- CNA agar media

Colony Appearance on Culture

- | Appearance | Microorganism |
|---|---------------------------------------|
| ◦ Medusa head, string of pearl colonies, inverted fir tree appearance | --- B. anthrax |
| ◦ Daisy head colony | --- C.diphtheria on tellurite media |
| ◦ Satellite colony | --- H. influenzae |
| ◦ Stalactite growth in ghee broth | --- Y. pestis |
| ◦ Checkers media | --- Strepto. pneumoniae on blood agar |
| ◦ Thumb print appearance, mercury drop colony | --- Bordetella pertussis |
| ◦ Fried egg colony | --- Mycoplasma |
| ◦ Draughtsman appearance | --- Pneumococcus |

→ CLED (Cystine, Lactose, Electrolytes Deficient) media is used to isolate and differentiate urinary tract bacteria, since it inhibits Proteus species swarming and can differentiate b/w lactose fermenters and non-fermenters.

→ Borrelia Burgdoferi can be grown in modified Kelly's medium.

→ Leptospira --- semisynthetic media such as EMJH, Stuart's, Korthoff's media, Fletcher medium is used for isolation.

→ A special media containing mannitol, egg yolk, phenol red, polymyxin, agar (MYPA medium) is used for isolation of B. cereus from feces and other sources.

→ Borrelia Burgdoferi can be grown in modified Kelly's medium.

→ Thayer Martin media contain vancomycin, colistin, nystatin, (NVC)

→ Modified Thayer Martin media contain NVC + trimethoprim

Flagellae

Flagellae	Found in
Single Polar (Monotrichus)	Vibrio, pseudomonas, legionella, spirochcates
Peritrichate	E coli, Salmonella, Proteus, Listeria, Bacillus Cl. tetani
Amphitrichus	Listeria
Lophotrichous (Polar tuft)	H. pylori (7 sheathed), V. parahemolyticus (single sheathed) Campylobacter, Spirilla

NUMERICALLY NAMED DISEASES

- 1st disease - Measles (Rubeola)
- 3rd disease - 3 day Measles (Rubella)
- 3 day fever - Sandfly fever
- 5th disease - Erythema infectiosum by Parvo B19 [Fundamentally for fifth]
- 5th day fever - Typhoid
- 6th disease - Exanthema subitum/roseola infantum by HHV 6 [remember six for subitum]
- 7 yr itch - Scabies
- 8th day disease - Tetanus
- 100 days cough - Pertussis

→ HIV (AIDS) is also k/as slim disease

→ Rubella is also k/as 3 day measles

IMP. FEVERS

Fever type	Caused by
Hemorrhagic fever	Ebola virus, Dengue virus etc.
Hemorrhagic fever with renal syndrome	Hantaan virus
Brazilian hemorrhagic fever	Sabia virus
Glandular fever	Ehrlichiosis
Undulant /Malta fever	Acute brucellosis
Pontiac fever	Legionella
Mediterranean spotted fever (Boutonneuse fever)	R. conorii
Familial mediterranean fever	X-linked R, autoinflammatory

Exotoxin Vs Endotoxin

	Exotoxin	Endotoxin
Secreted by	Bacteria	Cell wall component
Chemically	Polypeptides	Lipopolysaccharide (LPS)
Coded by	Plasmid	bacterial chromosome
Antigenicity	Highly antigenic	Less
Specificity	Highly specific, often enzymatic action	Generalised effect → fever & shock
Synthesis of antitoxin (protective Ab)	Yes	No
Can be toxoided	Yes	No
Heat sensitivity	Delicate/ heat labile	Resistant

→ Exotoxins are produced by Gram⁺ & some Gram⁻ bacteria (e.g. Shiga's dysentery bacillus, vibrio ETEC, pertussis pseudomonas) in contrast to endotoxin which are produced by only Gram⁻ bacteria

→ Enterotoxins :

Heat labile (Clostridium perfringens)

Heat stable (B. cereus, Y. enterocolitica, Staph.)

Important Growth Factors

Rotavirus	: Tryptophan
E. Coli	: Arginine
S. typhi	: Tryptophan
Gonococci	: Glutathione
Legionella	: L- Cysteine
Mycoplasma	: Cholesterol
Vibrio parahaemolyticus	: Normal saline
Atypical Mycobact	: Aryl Sulphate, Amide
Vibrio cholerae	: Saline
T.B., M. microti	: Niacin
H. Influenzae	: Factors V & X
M. hominis	: Glycerol
M. Haemophilum	: Factor X

◦ Growth factors required for

1. H. Parainfluenzae --- factor V (in Para P for Paanch)
2. H. Ducreyi --- factor X (in Ducreyi D for Dus)
3. H. influenzae --- factor V & X both [Factor V = NAD, X = Hemin]

◦ Iron is required for the growth of

Shigella, Neisseria, C. Diphtheriae

◦ Vit B6 required for growth of

Group D streptococci (viridans)

Major Capsulated (Encapsulated) Organisms

Streptococcus pneumoniae (Pneumococcus), Klebsiella, H. influenzae, pseudomonas, Neisseria, Cryptococcus [mnemonic : Some Killers Have Pretty Nice Capsules]

Non-motile, Non-spore, Non-capsulated organisms

- M. Tuberculosis
- Actinomycetes
- C. Diphtheriae
- Rickettsiae
- Shigella dysenteriae type I (all other shigella are motile)
- N. Gonorrhoeae [Mnemonic: Train GARDS]

AFB+/+ve Zeihl Nelson staining

- Nocardia (weak⁺) ◦ Mycobacteria
- Bacterial spores ◦ Cryptosporidium
- Isospora (coccidiosis) ◦ Legionella micdadei
- Rhodococcus ◦ Sperm head

(Mnemonic : MILANSSAR)

Imp. Gram +ve & Gram -ve bacteria

Gm ⁻	Gm ⁺
◦ Spirochetes	◦ M. Tuberculosis
◦ Rickettsiae	◦ Actinomycetes
◦ Chlamydia	◦ Nocardia, filamentous bacteria
◦ Mycoplasma	◦ Streptomyces Gm ⁻ cocci
◦ Acinetobacter	◦ Lactobacillus
◦ Moraxella, Neisseria	◦ Sarcina, Micrococci
	◦ Some bacilli like
	MACDONALD

→ All cocci are gram +ve except Neisseria & Moraxella

→ All bacilli are gram negative except MACDONALD:

(Mycobacterium tuberculosis, Anthrax, Clostridium, Diphtheria, Nocardia, Actinomyces, Listeria, Diphtheroids) are Gram +ve rods/bacilli

→ In Gm⁺ Spore forming are anthrax & clostridia, while non spore producing Diphtheria & Listeria.

UREASE +VE ORGANISMS

- Klebsiella
 - Proteus (proteus inconstans -ve)
 - Staph aureus
 - Cryptococcus
 - Diphtheroids
 - Ureaplasma urealyticum
 - H. Pylori, H. Influenzae
 - All Mycobacteria (typical & atypical) except MAI
- (Mnemonic : K.P. Saxena Ki CD ultimate Hai)

Catalase +ve organisms

- Shigella,
- Vibrio,
- Staph.

Types of motility of organisms

- Darting/vibratory motility
(Swarm of gnats) - Vibrio (fish in stream)
- Scintillating movt
(in hanging drop preparaⁿ) - Vibrio
- Swarming motility - Cl. tetani (Gm⁺)
Proteus (Gm⁻)
- Tumbling motility - Listeria monocytogenes
- Stately motility - Clostridia, E.coli,
salmonella
- Spinning motility - Fusobacterium gyrans.
- Cock screw - Spirochetes

→ School of fish appearance is seen in --- H. ducrei

→ Fish in stream pattern is seen in --- V. cholerae

Virulence factors

- Staph aureus - Coagulase⁺ } Both promotes virulence by
- Streptococci - M-protein } inhibiting phagocytosis
- Neisseria - Pili (facilitate adhesion to mucosa
& promotes virulence by inhibiting
phagocytosis)
- E. coli - P. pili
- Pneumococci - Capsular polysaccharide
- B. fragilis - Capsular polysaccharide
- H. influenzae - Capsule
- Tubercle bacilli - Cord factor
- Cl. welchii - Lecithinase
- B. pertussis - Filamentous hemagglutinin

Basis of typing / Classification

- Streptococci : Carbohydrate -C (Lancefield classification)
- Salmonella : O & H antigens (mainly O Ag)
- Enterobacteria : Lactose fermentation
- Shigella : Mannitol fermentation
(Shigella dysentery Mannitol^{-ve})
- Meningococci : Capsular polysaccharide Ag
- Influenza virus : Ribonuclear protein Antigen (A,B,C)

→ Shigella dysenteriae is mannitol non-fermenter, non-motile, exotoxin producing

BACTERIA AND THEIR CHARACTERISTICS, INFECTIONS, TOC

Bacteria	Species	Microbiological/ biochemical characteristics	Most commonly implicated in	Remark/ TOC
Gram +ve				
Staphylococci				
		Catalase ⁺ (all staphylococci)		
	<i>S. aureus</i>	coagulase ⁺	Surgical wound infections, Folliculitis, bullous impetigo, osteomyelitis	Clox
	<i>S. epidermidis</i>	coagulase ⁻	IV canula related, prosthetic	Vanco (for MRSA)
Streptococci				
		Catalase ⁻ (all streptococci)		
	<i>S. pyogenes</i>	Bacitracin sensitive, PYR ⁺	Sore throat, Acute rheumatic fever Cellulitis, Impetigo, Necrotising fasci- tis, Erysipelas (NICE)	
	<i>S. faecalis</i> (enterococci)	Growth in 6.5% NaCl, survives at 60 ^o temp		
	<i>S. viridans sanguis</i>	Optochin resistant, colonies insoluble in bile	Infective endocarditis	
	<i>S. viridans mutans</i>	"	Dental carries	
Pneumococcus				
	<i>S. Pneumoniae</i>	bile soluble Catalase ⁻ Oxidase ⁻	Meningitis in adults Otitis media Sinusitis lobar/ broncho pneumonia, OPSI Peritonitis in nephrotic syndrome	Ceftriaxone Amox
Corynebacteria				
	<i>Corynebacterium diphtheriae</i>	Meta chromatic granules (Volutin/ Babes Ernst granules) Polar bodies Albert Neissl's Stain ⁺ Chinese letter pattern Löffler's serum slope, Tellurite blood agar, Shows lysogeny/ phase conversion	Faucial diphtheria is m/c form Exotoxin inhibits protein synthesis	Pen/ erythro
Neisseria				
	<i>N. meningitidis</i> (Meningococci)	Kidney bean shaped, Diplococci Strict aerobes, capsulated	Meningitis, septicemia	Ceftriaxone
	<i>N. gonorrhoeae</i> (Gonococci)	Kidney bean shaped, Diplococci Contain pili	Gonorrhea (1st affects cervix), urethritis	Ceftriaxone/ Doxy
Anthrax Bacilli				
	<i>Bacillus Anthracis</i>	Motile with peritrichous flagella Bamboo stick appearance, Medusa head colony Mc Fadayen's reaction +ve PLET medium	Anthrax - Pulmonary (Wool Sorter's d/s) - Cutaneous (Hide porter's d/s)	Pn
Clostridia				
		Anaerobes, grow in Robertson's cooked meat media		

Bacteria	Species	Microbiological/ biochemical characteristics	Most commonly implicated in	Remark/ TOC
	<i>C. Perfringes/welchii</i>	Capsulated, non-motile, Stormy fermentation, Target hemolysis /double zone, Heat labile entero-toxin(α -toxin), Reverse CAMP test Nagler reaction (d/to lecithinase)	Gas gangrene (α toxin) Food poisoning (entero toxin) Necrotising enteritis (β toxin of Type C)	Pen + Clinda
	<i>C. tetani</i>	Drum stick appearance, Obligatory anaerobes	Spastic descending paralysis (Tetanus)	
	<i>Cl. botulinum</i>	Proteolytic, Swarming motility	Botulism (Diplopia is first manifestation, Flaccid descending paralysis) Food poisoning (No diarrhoea, constipation +) Infant botulism d/to honey (floppy baby)	
	<i>Cl. difficile</i>		Antibiotic associated diarrhoea (Pseudomembranous enterocolitis)	

Gram -ve

Klebsiella pneumoniae		Short bacilli, capsulated, urease ⁺	Pneumonia , UTI	Ceftriaxone
Proteus		Non capsulated pleomorphic motile rods, urease ⁺	UTI	
Shigella		Non motile nonsporing non capsulated	Dysentery, HUS	
Salmonella		Motile with peritrichate flagella		
	<i>S. typhi</i>	Anaerogenic	Enteric fever	Ceftriaxone
	<i>S. paratyphi</i>	—	paratyphoid fever	
Vibrio	<i>V. cholerae</i>	Comma shaped motile organism (fish in stream app.)	Cholera	
	<i>V. parahemolyticus</i>	Kanagawa phenomena is seen		
Campylobacter	<i>C. jejuni</i>	Non-sporing, motile	GI infections, typhoid like illness	
Pseudomonas		Aerobic, motile	Nosocomial infections, Burn wounds, Malignant otitis externa	
H. influenzae		Non motile, non sporing in infants Cocobacilli. 5% CO ₂ supplement. Requires X factor (haemin) and V factor (NAD) for growth on chocolate agar	Meningitis, pneumonia	

Bacteria	Species	Microbiological/ biochemical characteristics	Most commonly implicated in	Remark/ TOC
Bordetella	<i>Bordetella pertussis</i>	Pleomorphic, aerobic bacilli	Pertussis	Macrolides (Erythro/ azi- thro)
Yersinia	<i>Y. pestis</i>	Ovoid bacilli Safety pin appearance Stalacite growth in ghee broth	Plague	Tetracycline
	<i>Y. enterocolitica</i>	D/g by stool culture	Yersiniosis	self resolving
	<i>Y. pseudotuberculosis</i>	Zoonotic, Urease +ve, virulence factor pYV	Far East scarlet-like fever, pseudo- appendicitis, erythema nodosum, ReA	
Brucella melitensis		Coccobacilli, milk ring test Castaneda method	Brucellosis (Undulant fever)	Doxy, strepto
Ehrlichia		Atypical organism	Ehrlichiosis	Doxy
Borrelia		Modified Kelly's medium (BSK)	Lyme d/s (Borreliosis)	Doxy > Amox
Bacteroid fragilis		Non-sporing, anaerobes, normally present in colon	Brain abscess, abdominal abscesses (Never a/w septicemic shock)	Metro
T. Pallidum		Motile, delicate spirochete, Negative staining with India ink/phase con- trast microscopy, Stained with prolonged Geimsa stain	Syphilis	Pen

Bacteria and their alternate names

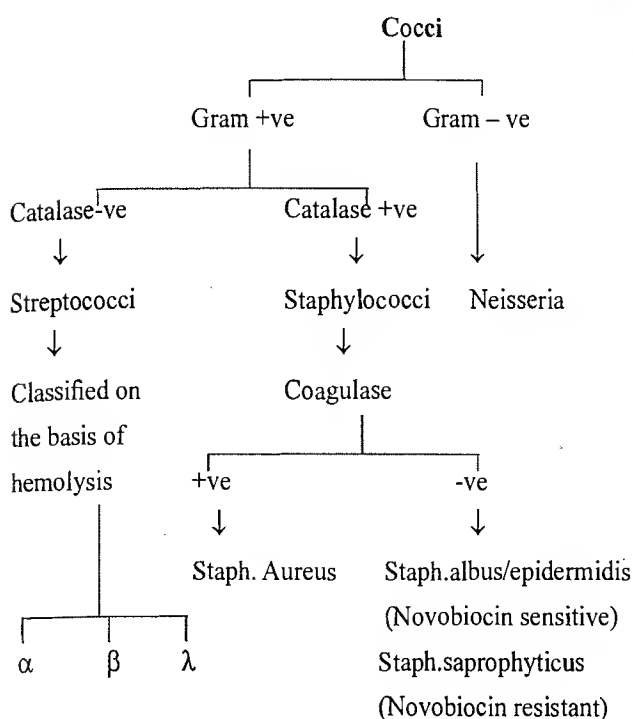
- Bordetella Bordet Gengou bacillus
- Clostridium tetani Nicolaire's bacillus
- Corynebacterium **Klebs-Loeffler's bacillus**
diphtheriae
- Corynebacterium **Preisz-Nocard bacillus**
pseudotuberculosis
- Haemophilus aegypticus Koch-Weeks bacillus
- Haemophilus influenzae Pfeiffer's bacillus
- Klebsiella pneumoniae Friedländer's bacillus
- Klebsiella ozaenae Abel's bacillus
- Klebsiella Rhinoscleromatis Frisch's bacillus
- Mycobacterium tuberculosis Koch's bacillus
- Mycobacterium Bathey's bacillus
intracellulare

- Mycobacterium Johne's bacillus
paratuberculosis
- Mycoplasma Eaton agent
- Pseudomonas pseudomallei Whitmore's bacillus

Sterile Pyuria

- Chlamydia, HSV,
- Cyclophosphamide
- TB (with acidic urine)
- Fungal infections
- Renal stones, renal papillary necrosis
- Cancer bladder/urinary tract
- *Ureaplasma ualyticum*

Approach to a patient with infection with cocci



Streptococci : Classification on the Basis of Hemolysis

Type of hemolysis	Color of colony	Lancefield group & Biochemical features	Bacteria
Partial α	Green	Optochin sensitive, Soluble in bile	<i>S. pneumoniae</i>
		Optochin resistant, Not soluble in bile	Viridans streptococci
Complete β	Clear	Gp A, Bacitracin sensitive	<i>S. pyogenes</i>
		Gp B, Bacitracin resistant	<i>S. agalactiae</i>
No hemolysis γ (Indifferent streptococci)		Gp D, PYR +ve, Growth in 6.5% NaCl	Enterococcus (<i>S. faecalis</i>)
		Gp D, No growth in 6.5% NaCl	<i>S. bovis</i>
		Anaerobes	Peptococci

Some medically important Streptococci

Streptococci	Gp	Hemolysis	Habitat	Disease
<i>Pyogenes</i>	A	β		Rheumatic fever AGN
<i>agalactiae</i>	B	β		Neonatal meningitis
<i>equisimilis</i>	C	β		Pharyngitis, Endocarditis
<i>mutans</i>				Dental caries
<i>faecalis</i>	D	γ >> α, β	Colon	UTI, endocarditis
<i>milleri/anginosus</i>	F	α, β	Throat, Colon, FGT	Pyogenic infections brain abscess
<i>pneumoniae</i>	None	α	Throat	Pneumonia
<i>viridans</i>		α	Mouth, throat	Dental caries

Streptococci exhibit some common properties:

1. All are catalase +ve
 2. They are not soluble in bile (except pneumococcus)
 3. They ferment sugars /ribose (except *s. pyogenes*)
 4. Most of them hydrolyze PYR (except *s. anginosus*)
- *S. agalactiae* (Gp B streptococci) is c-AMP +ve.

Streptococcal Toxins

- Streptolysins S and O are produced by hemolytic streptococci group A and C
- Streptodornase (DNAase) : Type B is most antigenic.

Clostridia

	Lecith C	Lip	Lac (saccharolytic)	Prot (proteolytic)
<i>C. perfringens</i>	+	-	+	-
<i>C. botulinum</i> type ABC	-	+	-	+
type CDE	-	+	-	-
<i>C. tetani</i>	-	-	-	-
<i>C. septicum</i>	-	-	+	-
<i>C. difficile</i>	-	-	-	-

Saccharolytic : *C. welchii*, *septicum*,
(turns meat → pink) edematous, chauvoei

Proteolytic : *C. sordelli*, *sporogenes*,
(turns meat → black) Histolyticum, *botulinum* A,B,F

HACEK Group of organisms

- H ---- Haemophilus spp.
 A ---- Actinobacillus actinomycetemcomitans
 C ---- Cardiobacterium hominis
 E ---- Eikenella corrodens
 K ---- Kingella kingae

El tor Vibrio

In comparison to classical cholera vibrio hemolysis, VP reaction, and chick embryo agglutination are +ve and polymyxin B sensitivity and group IV phase susceptibility are -ve in Eltor.

[Mnemonic: Elton was HCV +ve but p4 -ve]

Atypical Mycobacteria

Reaction	Typical		Atypical mycobacteria
	M. Hominis	M. Bovis	
Niacin formation	+	-	Usually -ve (M. Simiae +, M. Microti ± M. Chelonae ±)
Nitrate reduction	+	-	M. Kansi, Fortium phlei, smegmatis +ve
Catalase positivity (Provides INH sensitivity)	+	+	+++
Peroxidase	+	-	-

- Aryl sulfatase & amidase test +ve only in Atypical mycobacteria
- All mycobacteria (typical & atypical) urease +ve except: MAI which is urease -ve.
- Skin pathogens
 - M. ulcerans - only known toxin producing mycobacteria, causes Buruli ulcer
 - M. Marinum (M. balnei) - Causes low grade tuberculin reaction, swimming pool granuloma
- Scotochromogens (M. Scrofulaceum, M. Phlei)
 - Atypical mycobacteria which change color
 - Produces pigment in dark but capable of also producing pigment in light (also photo chromogen)
- Photochromogens : M. Kansi and M. Marinum.
 [Mnemonic: Kansi & Maya together had a photo shot]
- Non-pathogenic mycobacteria - M. Smegmatis & M. phlei (rapid growers), M. stercoris
M. tuberculosis causes--- Lupus vulgaris, scrofuloderma
- Contaminated water used for washing endoscopes will lead to infection with mycobacterium chrolonae.

Drug (Antibiotic) Resistance Among Microbes

- M/c mechanism of DR is : drug inactivation
- Commonly acquired by lateral or horizontal gene transfer (HGT) of RTF from donor cells (by transformation, transduction or conjugation)
- DR transmitting factor in bacteria is : Plasmids
- Penicillin resistance in pneumococcus is d/to alteration of PBPs by transformation & horizontal DNA transfer.
- Vanco & Teicoplanin resistance in enterococci is d/to alteration of DADL or DADS target d/to lack of critical site for H₂ bonding.
- Resistance in methotrexate is d/to overproduction of DHFR.

RICKETSSIA

- Obligate intracellular parasites which do not grow in cell free cultures. They multiply within living cells (*Exception is Ro. quintana which can grow in blood agar*)
- Gram -ve (poorly stained) pleomorphic rods, non motile, non capsulated. They take Giemsa and Castaneda stains
- Posses cellwall (containing muramic acid)
- Posses both DNA & RNA
- They are not seen with naked eye c/b seen under light microscope.
- Divide by binary fission.
- A/w rashes becoz organism multiply in vascular endothelium.
- Several Rickettsia possess antigen that cross reacts with antigen of OX-strains of proteus vulgaris.
- Serology is used in the d/g of rickettsial d/s. Weil-Felix reaction is simple and useful tube agglutination test in which sera are tested for agglutinins to the O antigen of proteus vulgaris strains OX -19 & OX -2 & proteus mirabilis (OX-K)
 - WF reaction is positive mainly in typhus group
 - Epidemic & endemic typhus agglutinate (+++) with OX-19
 - Tick borne spotted fever agglutinate (++) with both OX-19 and OX-2
 - Scrub typhus agglutinate strongly (+++) with OX-K
 - WFR is negative (of no value) in pox, Q-fever & trench fever (mnemonic Poqet for Pox, Q-fever & trench)
- Transovarian transmission is seen in mite borne rickettsial infections e.g. scrub typhus, rickettsial pox, tick typhus
- Rickettsiae are susceptible to tetracycline (DOC) but not to penicillin & sulfonamides.

Group	Disease	Causitive agent	Insect vector	Reservior	WF reaction	Comment
Typhus fever group	• Epidemic/classic t~ (Jail fever/ Brill-zinzer d/s)	<i>R. Prowazeki</i>	Body louse	H	+++OX-19	Transmitted by pediculosis corporis and capitis
	• Murine/ endemic t~	<i>R. Typhi (mooseri)</i>	Rat flea	R	+++OX-19	<i>Tunica reaction</i> +ve
	• Scrub typhus	<i>R. Tsutsugamushi</i>	Trombiculid mite (chiggers)	R	+++OX-K	'Punched out' ulcer + black eschar Rash, fever, lymphadenopathy Adult mite feeds on plant Doxycycline is DOC
Spotted fever group	• Rickettsial pox	<i>R. akari</i>	Mite	Mice	- ve OK-K	All spotted fever are transmitted by hard ticks except 'pox' (by mite), Least dangerous
	• Indian tick typhus	<i>R. conorii</i>	Ixodid ticks	R, dogs		Also k/as Mediterreanean spotted fever
	• RMSF	<i>R. rickettsii</i>	Ixodid ticks	R, dogs		Most severe form
Others	• Q-fever	<i>Coxiella burnetii</i>	No vector (air borne)	Cattle, Sheep, goat	- ve WFR	Zoonotic d/s transmitted by contaminated animal milk. urine feces, placenta. Never cause rash or local lesion No vector (but extrahuman tick vector is known)
	• Trench fever (5 days fever)	<i>Rochalimaea/Bartonella quintana</i>	Louse	H		Only rickettsia which c/b cultured
	• Ehrlichiosis	<i>Ehrlichia</i>	Tick	H		

[R= Rodents, H= Human]

Salmonella typhi Antigens

H-antigen	O-antigen	Vi-antigen
• Heat labile, strongly immunogenic	• Heat stable, Virulence factor	• Used in epidemiological typing
• Flagellar Ag	• Somatic cell wall Ag	• Cellwall antigen
• Antibody to H antigen appears first & persists longer	• More in diseased person	• Absence of Ab to this Ag indicates poor P/g
• +nt in Dreyer's tube (conical bottom)	• Used for classification	• Prevents the agglutination of S.Typhi with "O" Ag
	• +nt in Felix tube (round bottom)	

Non typhoid salmonella

- Important cause of self limiting gastroenteritis.
- Essentially animal parasites, but can cause food poisoning.
- Examples: *S. enteritidis*, *S. typhimurium*, *S. Heidelberg*, *S. Newport*, *S. javiana*.
- Ubiquitously present in the environment and reside in the GIT in animals.
- Eggs and poultry products are m/c source of infection.
- D/g : Isolation of organism from freshly passed stools.

Mechanism of action of some toxins

Toxin	M/A
• Strychnine	• <u>Post synaptic</u> inhibition of NT glycine in spinal cord. • Acts on AHC of spinal cord and inhibits post synaptic potential leading to release excitation
• Botulinum	• Inhibits release of Ach from peripheral nerves (N_M Junction /presynaptic) • Preformed/intra-dietic toxin which causes symmetric descending flaccid paralysis
• Tetanus	• Toxin is tetanospasmin which inhibit presynaptic release of NT glucine & GABA in CNS • Toxin acts on motor end plate; spinal cord, brain, sympathetic NS (but does <u>not</u> /rarely act on parasympathetic system)

- Cholera toxin, diphtheria toxin, pertussis toxin, *E. coli* heat-labile toxin, and *P. aeruginosa* (exotoxins A, S, and T) have adenosine diphosphate (ADP)-ribosyl transferase activity → activate c-AMP
- Diphtheria toxin inhibits protein synthesis by inactivating EF-2.
- Toxins inhibiting protein synthesis :Diphtheria, pseudomonas, shiga toxin.

Mechanism of Diarrhea

Inhibit Na ⁺ K ⁺ ATPase	↑c-AMP	↑c-GMP
<ul style="list-style-type: none"> o Rota virus (Secretory diarrhea) 	<ul style="list-style-type: none"> o Cholera o ETEC-labile toxin o Staph. aureus o Salmonella o Bacillus cereus o Carcinoid o Medullary Ca thyroid 	<ul style="list-style-type: none"> o E. histolytica o ETEC - stable toxin o Clostridium difficile

[Mnemonic for ETEC labile toxin: HLA- Heat Labile by AMP]

Traveller's Diarrhoea

- o M/c cause - ETEC
- o M/c cause in southeast Asia and Africa - Campylobacter
- o M/c virus a/w T~ : Rota & Norwalk

Cholera toxin

- o Active subunit is A1 which upregulates adenylcyclase activity causing irreversible ADP ribosylation of GTP binding protein (cAMP acts as second messenger). B subunit is pentameric binding subunit it binds GM gangliosides receptors

Diphtheria toxin

- o Produced by toxigenic or virulent strains of *C. diphtheriae*. About 90-95% gravis and intermedius strains are toxigenic, while only 80-85% of mitis are so.
- o Diphtheria toxin is a protein and very potent exotoxin. Consist of two functionally distinct polypeptide chains. Both fragments are required for toxicity
Fragment A --- N- terminal, It has enzymatic activity. It causes irreversible inhibition of protein synthesis by NAD⁺ dependent ADP ribosylation of EF-2 which results in cell death
Fragment B --- C- terminal, responsible for Binding the toxin to the cells. The antibody to fragment B prevents the binding of toxin to the cells and is thus protective.

→ Pertussis toxin also acts by ADP ribosylation

ENTEROBACTERIA

- o Features are :
 1. May or may not capsulated.
 2. Motile by peritrichate flagella or non-motile.

3. Aerobic and Facultatively anaerobic
4. Ferment glucose producing acid and gas or acid only.
5. Reduce nitrates.
6. Form catalase but does not form oxidases.
7. Non sporing, non-acid fast, G-ve bacilli.

Classification:

Properties	Motile	Non-motile
Lactose fermenter	E. coli	Klebsiella
Non-lactose fermenter	Solmonella Pseudomonas	Shigella, Proteus species,
Late-lactose fermenter	-	Shigella sonnei

- o *Enterobacter* are motile, capsulated, lactose fermenting bacilli, which are indole & MR-ve but VP & citrate + ve.

E. coli

- o ETEC
 - Heat stable toxin - ↑c-GMP
 - Heat labile toxin - ↑c-AMP
 } traveller's diarrhea
 [It produces cholera like enterotoxin (cholera infantum), Biken test⁺]
- o EPEC
 - Attaches to enterocytes (enteroadherent) & destroy brush border villi (inflammation⁺)
 - Causes infantile diarrhea (remember EPEC affects pediatric population)
- o EIEC
 - Only E-coli which invades G.I. Mucosa (enteroinvasive) & produces dysentery like disease (toxin resembles shigella).
 - Sereny test⁺, growth in HeLa cell culture or HEP-2 cells
- o EHEC (VTEC)
 - Produces verotoxin or **verocytotoxin** (shiga like toxin) which acts on vascular endothelium & causes hemorrhagic colitis + HUS (Strain 0157)
 - Does not ferment sorbitol (sorbitol⁻)
- o Entero aggregated E coli (EAggEC)
 - Form a heat stable enterotoxin EAST1. It is a/w persistent diarrhoea in developing countries.

- Only EPEC affects pediatric population, rest all strains of E. coli can affect all age group
- Sereny test is an invasive test for shigella

ANTHRAX

Form of anthrax	Examples
• Cutaneous	1. Malignant pustule 2. Hide Porter's d/s
• Pulmonary	Wool sorter's d/s, Hemorrhagic pneumonia
• Intestinal	Invasive enteritis
• Anthracoid	Pseudoanthrax

Causative organism in

- Oraya fever -- *Bartonella bacilliformis*
Cat-scratch disease -- *Bartonella henselae*
- Trench fever -- *Bartonella quintana*
- Epidemic Relapsing fever-- *Borrelia recurrentis*
Endemic Relapsing fever -- *Borrelia duttonii*, *B. hermsii*,
B. parkeri
Lyme disease -- *Borrelia burgdorferi*
- Pontiac fever -- *Legionella pneumophila*
- Weils disease -- *Leptospira icterohemorrhagica*
- Undulant/ Malta fever -- *Brucella melitensis*
(Mediterranean fever)
- Rat - bite fever
- Sodoku -- *Spirillum minus*
- Haber-hill fever-- *Streptobacillus moniliformis*

MYCOPLASMA

- Mycoplasma are also k/as PPLO/ Eaton agent.
- Mycoplasma are
 - Smallest bacteria causing d/s in humans.
 - Have smallest genome.
 - Only bacteria which **does NOT** have cell wall. So no fix shape (L-forms are seen), they are not acid fast & not killed by penicillin or other β -lactams like cephalosporins [all these properties are attributed to cell wall]
 - Only bacteria which contain sterol in cell membrane.
- Can not be stained by Gram stain. Special stain "Diene's stain" is used.
- Biphasic & "Fried egg" appearance of colonies. Can be cultivated in cell free (artificial) media enriched with 20% horse / human serum + yeast extract.
- Gliding motility is seen.
- *M. pneumoniae* causes 1^o atypical pneumonia(walking pneumonia) in immunocompetent host. Cold agglutinins are +ve.
- *Ureaplasma urealyticum* causes NGU (Non-gonococcal urethritis). 2nd m/c cause of NGU after chlamydia.

N GONORRHOEAE

- Typically affect the epithelial cells of the urethra, vagina, cervix, fallopian tubes, endometrium, epididymis, rectum, pharynx, and the eyes of newborn babies.
- In the newborn babies typically affects eyes.
- Vaginitis is the m/c manifestations in prepubertal children.
- In males, primary site is urethra. Epididymitis can occur.
- In women, the initial infection usually involves the urethra & cervix. The vaginal mucosa is usually resistant to infection by cocci becoz of Stratified squamous epithelium. The infection may extend to Bartholin glands, endometrium & tubes.
- Fitz-Hugh-Curtis syndrome is perihepatitis + peritonitis, an extrapelvic complication of pelvic inflammatory disease.

CHLAMYDIA

- Obligate intracellular. they are filterable & do not grow in cell free media.
- Chlamydia are
 - Gram -ve bacteria.
 - Energy parasites/ ATP parasites.
 - Posses cell wall as in bacteria & rickettsia. Susceptible to antibiotics (esp to tetracycline)
 - Contains both DNA & RNA
- Elementary bodies (reticulate bodies) are present which are stained with iodine.
- Nucleic acid amplification test (NAAT) is highly sensitive and specific test. PCR is most sensitive while culture (McCoy cells) is most specific.
- *Chlamydia trachomatis* causes
 - Trachoma: M/c infectious cause of blindness in India (A-C strain)
 - NGU (m/c cause), endocervicitis in females, infantile pneumonia all these are caused by D-K strains
 - LGV by L₁-L₃ strains (Frei's test +)
- *Chlamydia pneumoniae*---- is found to be a/w atherosclerosis and CAD (MI).
- *Chlamydia psittaci*---- causes pneumonia in birds.
- TWAR strain causes ---- Acute respiratory disease.
- T/t: Tetracycline/macrolides.
Azithro for NGU.

Neisseria Vs Chlamydia Infections

	Neisseria	Chlamydia
• Presentation	Acute	Chronic ds
• Transport media	Amies media	Stewart media
• A/w	Recent menstrual flow	
• Cl/f	- Mucopurulent discharge - Lower abd pain, fever - Bartholin's abscess	- Mostly asymptomatic - Cloudy discharge ± - Urethritis, pyuria
• First affects	Cervix	
• Cultured on	Thayer Martin media (Selective media)	-ve urine culture
• T/t	Ceftriaxone	Doxycycline

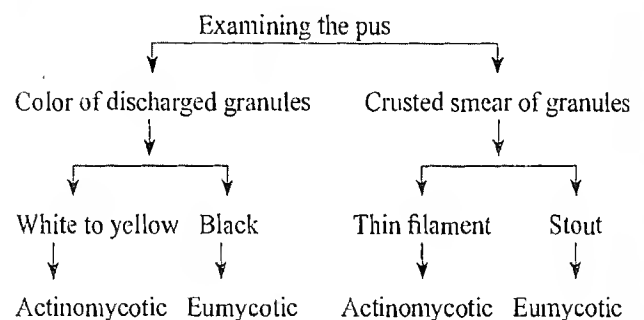
- Arthritis dermatitis syndrome may be d/to *N.gonorrhoeae*
 → Watercan perineum is seen in infection with *N.gonorrhoeae*
 → Waterhouse Fredrickson syndrome (DIC, MODS, purpura, adrenal h'age) is d/to is *N.meningitidis* shock.

ACTINOMYCOSIS Vs NOCARDIA

	Actinomycosis	Nocardia (aerobic)
Gram stain	Gram+filamentous branching	Gram+ filamentous branching
Acid fastness	NOT (AFB ⁻)	AFB + weak (but <i>N. madurae</i> AFB ⁻)
Morpho	Non-motile Non-sporing Non-capsulated	Non-motile Non-sporing Non-capsulated
Inhabitat	Normally found in oral/genital flora	Soil inhabiting (NOT an endogenous infection)
Infection in	In immunocompetent	Immunocompromised, HIV/AIDS
Cl/f	1. Oro-cervicofacial m/c type ↓ Woody/lumpy jaw 2. Appendix in GIT 3. PID in IUCD users (<i>A.israelii</i>)	Airborne inhala ⁿ → Lungs → profuse, thick sputum. CXR : Lt lower lobe nodule with central cavitation
Dx/ Microscopy	Spidery colony & Ray fungus, Creamy white granules or Sulphur granules (organism + pus)	Paraffin bait technique
• T/t	Penicillin	TMP-SMX/ sulfonamides

MYCETOMA

- Chronic granulomatous d/s.
- Involves s/c or deeper tissues destructing the cartilage, bone and fascia.
- M/c site is foot. Other sites are hand, gluteal region of thigh.
- 1st described in Madurai (Mycetoma Madurae/Madura foot).
- Presents as abscess, tumours with multiple sinuses discharging pus & sulphur granules (tightly clumped colonies of organism).
- Approach to Dx: Based on



- Causative organisms & color of grains

Caused by fungus (Eumycetoma) or bacteria mainly actinomycetes. (Actinomycetoma).

Eumycetoma (Fungal)	Color of grains	Actinomycetoma (Bacterial)	Color of grains
<i>Madurella mycetomatis</i>	Black	<i>Actinomyadura pelletieri</i>	Red
<i>Pseudallescheria (Petriellidium) boydii</i>	Pale	<i>Streptomyces somaliensis</i>	Yellow
<i>Acremonium falciformis</i> <i>Aspergillus flavus/nidium</i>	Pale	<i>Actinomyadura madurae</i>	Pale
<i>Exophiala jeanselmei</i>	-	<i>Nocardia brasiliensis/cavae/asteroides</i>	Pale

- Mycetoma like lesions (botryomycosis) is occasionally produced by *staph.aureus*

VIROLOGY

Structure of Viruses

- Usually all DNA viruses are double stranded(ds) & RNA viruses are single stranded(ss).

Exceptional ss DNA viruses are : Parvovirus

Exceptional ds RNA viruses are : Reovirus

- Naked (non-enveloped) DNA viruses*
Parvo, Adeno, Papova Viruses (PAP)
- Naked (non-enveloped) RNA viruses*
Picorna, Calci and Reoviruses (PCR)
- Segmented RNA viruses*
Bunya, Orthomyxo, Retroviruses, Arena (BORA)
- Viruses with negative strand*
Bunya, Orthomyxo, Paramyxo, Arena (BOPA)
- Viruses with helical symmetry*
Bunya, Orthomyxo, Corona, Arena (BOCA)
- Circular viruses are*
Bunya, Arena (ss RNA) and papovavirus (ds DNA)

→ Largest virus - pox virus (300 nm), smallest virus- parvo virus (foot & mouth disease virus 20nm) Largest RNA virus is Rhabdo & smallest RNA virus is Picorna

→ Smallest bacteria - mycoplasma

- Virusoid*: Nucleic Acid dependent on helper virus to package nucleic acid
- Viroids* : Plant pathogen consist of few hundred nucleotides (Single-stranded covalently closed circular RNA molecules). existing as highly base-paired rod-like structures without protein coat.
- Prions*: Abnormal cellular protein that can spread from cell to cell (JC-virus)
- Virion*: Extracellular infectious viral particle
- Elementary bodies* : Stained virus that can be seen by light microscopy ex. pox virus (largest virus)

Isolation of Micro-organisms/Viruses

- Chlamydia --- Yolk sac inoculation
- HBV --- Cell lines transfected with HBV DNA

Culture of Viruses

- Human fibroblast c/b used for the production of diploid cell strains of rabies vaccine (WI-38)
- Influenza vaccine c/b grown in allantois of chick embryo
- Rabies vaccine (flury strain) & yellow fever (17D strain) c/b grown in chick embryo.

Viruses that form pocks on CAM (chorioallantoic Membrane)

- Herpes
- Vaccinia (small pox)
- Variola
- Monkey pox
- Cowpox
- (but NOT in chicken pox)

Viral Inclusion Bodies

Inclusions	Found in
Intracytoplasmic eosinophilic	1. Negri bodies in Rabies 2. Guarnieri bodies in Small pox 3. Henderson-Peterson bodies in Molluscum contagiosum
Intranuclear acidophilic	1. Cowdry type A in Herpes simplex virus & Varicella zoster virus 2. Torres bodies in Yellow fever 3. Cowdry type B in Polio
Intranuclear basophilic	Cowdry type B in Adenovirus "owl eyes" in cytomegalovirus
Both intranuclear & extranuclear / intracytoplasmic	Warthin finkeldey bodies in Measles

Properties of viruses

- Hepatitis & polio viruses are relatively resistant to chlorination.
- Sunlight UV-rays, ionizing radiation, Organic I₂ compounds are virucidal.
- Formaldehyde, B. propiolactone are employed for synthesis of killed viral vaccines
- Cytopathic effects of viruses*:
 - Syncytium (giant cell) formation : Measles, RSV
 - Rounding of cells : Picorna
 - Cell necrosis & lysis : Entero
- Viral hemagglutination**
Agglutination of RBCs by viruses as in *Influenza virus*
- Reassortment**
Seen in reoviruses (e.g. rotavirus, ortho-reovirus, orbivirus, and coltivirus) and other segmented RNA viruses (*Influenza A virus*)
- Elution** :
Cholera vibrio posses RDE receptor destroying enzymes which leads to release of virus from RBC surface & reversal of hemagglutination. Seen in *Influenza virus* + parainfluenza, Mumps, NDV

◦ Hemadsorption

Seen in Myxo viruses, influenza, para-influenza, Mumps

Herpes virus

- Latent infection is characteristic of herpes group of viruses & site of latent infection is as follows-

Type of HHV	Site of predilec ⁿ	D/s
◦ HHV-1/HSV-1	Neurons, Trigeminal ganglia	Mucosal, eye, CNS d/s
◦ HHV-2/HSV-2	Neurons, genitalia	Genital lesion
◦ HHV-3/VZV	Neurons, sensory ganglia	Chicken pox, Zoster
◦ HHV-4/EBV	Lymphoid tissues	IM, Burkitt's
◦ HHV-5/CMV	Salivary glands, kidney	Mononucleosis like syndrome, Hemorrhagic retinitis in AIDS pt, pneumonia in organ transplant pt.
◦ HHV-6	Lymphoid tissues	Roseola infantum, 6th d/s multiple sclerosis
◦ HHV-7	Lymphoid tissues	
◦ HHV-8	-	Kaposi's sarcoma

Varicella Zoster Virus (VZV)

VZV causes 2 distinct clinical d/s

1. Primary infection with VZV in non-immune individuals causes --- **Chickenpox**
2. Reinfection with VZV in immunocompromised individuals causes --- **Herpes Zoster(Shingles)**

Herpes zoster is d/to reactivation of virus in sensory ganglia (e.g. trigeminal ganglion) seen in old age.

- Residual pain/ neuropathic pain in dermatomes of affected sensory ganglia is k/as → **Postherpetic neuralgia**.
- When VZV involves ophthalmic division of 5th nv. or nasocilliary nerve → **Ophthalmic zoster** (Herpes zoster ophthalmicus) occurs.
- When VZV involves facial nv. (Reactivation of VZV in the geniculate ganglion) it is a/w eruptions on ipsi/L tympanic membrane / EAM (external auditory meatus), facial palsy often a/w loss of taste in the anterior tongue, tinnitus, hearing loss and vertigo - k/as Ramsay Hunt syndrome

Adeno Viruses

- ds DNA virus . 47 serotypes are there:

- Diseases d/to various serotypes:

Type 3, 7, 14 --- Pharyngo-conjunctival fever
(Swimming pool conjunctivitis)

Type 8, 19, 37 --- Epidemic kerato-conjunctivitis/
Shipyard eye

Type 11, 21 --- Hemorrhagic cystitis

Type 3, 4, 7 --- Pneumonia

Type 40, 41 --- Diarrhoea

Coxsackie Viruses

- Coxsackie A 24: acute hemorrhagic conjunctivitis.
- Coxsackie B: Myocarditis, pericarditis & epidemic pleurodynia (Bronholve's d/s)
- Other coxsackie d/s : **Herpangina**, Hand foot & mouth d/s.

Entero Viruses

EV - 68 ----- Causes pneumonia and bronchitis in children

EV - 69 ----- Not a/w any human disease

EV - 70 ----- Causes acute **hemorrhagic conjunctivitis**

EV - 71 ----- Originally isolated from meningitis and encephalitis, HFMD

EV - 72 ----- Hepatitis (also K/as HAV)

→ *Enteroviruses do not cause hemorrhagic fever.*

→ *Slapped cheek appearance is seen in erythema infectiosum, infection caused by parvo B19*

→ *HPV infection found only in humans*

Rotavirus

- Encapsulated virus of Reoviride family which contains segmented **ds RNA** genome (**SPLIT GENOME**)
- **M/c cause of diarrhea in infants.**
- Anti-rotavirus antibodies are found in mother's milk so infection is frequent at the time of weaning. Affects 6 month - 2 years children.
- Invade & destroy mature epithelial cells in middle & upper villous (*Terminal ileum villi*)
- Diarrhea is d/to ↓ed absorption of Na⁺ & H₂O from bowel lumen (*Osmotic diarrhea*)
- Minimum infective inoculum :- 10 particles
Infected individual sheds :- 10¹² particles/ml stool.
- IP is 2 days f/ by vomiting & then secretory diarrhea
- Infection is common in winter & fall.
- Virus can not be cultured except group A.

HPV

- Non cultivable virus.
- HPV-1 & 4 : Cause skin & plantar warts
- HPV-6 & 11: Low risk type , sexually transmitted & cause genital warts (Condyloma acuminatum)
- HPV-16 & 18 are high risk type and cause CIN, cancer cervix (50% by HPV-16 & 25% by HPV-18) , cancer penis and anus.
- Males do not have any significant d/s.
- Best test for d/g: Hybrid capture technique for DNA.
- For screening: Pap smear is useful
- Vaccines:
 - Bivalent : Contain 16,18 (Cervarix)
 - Tetavalent : Contain 6, 11,16,18 (Gardasil)

Antigenic Drift & Shift in Influenza

Properties	Antigenic Drift	Antigenic Shift
1. Definition	Gradual/ sequential change in antigenic structure occurring at frequent intervals.	Sudden, drastic, discontinuous variation in antigenic structure.
2. Due to	Point mutation under selection pressure of community.	Genetic reassortment of human with avian/ animal viruses → antigenic variation.
3. A/w	Type A or B	type A (rarely B)
4. Responsible for	Small periodical epidemics.	Major epidemics & pandemics.

- In influenza virus antigen variation occurs mostly in Type A. ($A > B > C$) . Influenza type C is antigenically stable or antigen variation does not occur.
- Seasonal influenza is caused by H3N2 or H1N1
- Pandemic influenza is caused by Novel H1N1 (Swine flu).
- Highly pathogenic avian influenza is caused by H5N1 (Bird flu).
- In polio virus
 - P_1 is responsible for most epidemics [most common],
 - P_2 is most effective antigen (most immunogenic), eradicated
 - P_3 causes most cases of VAPP (vaccine associated paralytic poliomyelitis)

Slow Virus Diseases

Gr.	D/s	Host	Viruses
<i>Animal infections</i>			
A	Visna	Sheep	Retrovirus, HIV related
A	Maedi	Sheep	Retrovirus, HIV related

B	Scrapie	Sheep	Prion
B	Mink encephalopathy	Mink	Prion
<i>Human infections</i>			
B	CJ disease	Man	Prion
B	Kuru	Man	Prion
B	Gerstman- Strassler Scheinker Syndrome	Man	Prion
B	Fatal familial insomnia	Man	Prion
C	SSPE	Man	Measles, Rubella virus
C	PML	Man	Papova (Polyoma) virus

- Progressive Multifocal Leukoencephalopathy (PML) is a rare subacute demyelinating d/s seen in immunocompromised elderly & HIV+ve patients. There are cytologic changes in both astrocytes and oligodendrocytes which contain viral inclusions of JC polyomavirus (papova viridae family).
- In Creutzfeldt - Jakob disease (CJ disease) there is astrocytosis, spongiform vacuolation /transformation of the cerebral cortex and deep grey matter structures (caudate, putamen nucleus)
- Corneal transplant may spread CJ disease
- Sub acute spongiform viral encephalopathy (SSVE) is also k/ as bovine spongiform encephalopathy or Mad cow disease.

MYCOLOGY

- Fungi are eukaryotic.
- Fungi have rigid cell wall. Major structural polymer in fungal cell walls is typically made up of **chitin**.
- They are chemotrophic.
- They are cultured on Sabouraud's agar with antibiotics such as gentamycin, chloramphenicol, cyclohexide, Corn meal agar. (Rhizopus can not be cultivated & Malassezia furfur difficult to cultivate).
- Fungi imperfecti/Deuteromycetes** - No sexual reproduction found e.g. candida albicans, Coccidioides immitis.
- Budding yeast cells are: Fungus which multiply by budding
 - True yeast: Cryptococcus
 - Yeast like organism :Candida (single celled)
 - Dimorphic fungi: Sporothrix
- Septate hyphae are seen in Aspergillus and many other species have septate hyphae. **Aseptate or coenocytic (without septa) Non-septate hyphae** are a/w Mucor, some zygomycetes, and other fungi

Important Fungi

Aspergillus

- Septate hyphae⁺ with dichotomous branching at acute/narrow angle (45°)
- Fruiting bodies⁺ with conidia
- Invades blood vessels, causes hypereosinophilia.
- M/c cause of invasive A~ is *A. fumigatus*. Seen in DM
- Allergic bronchopulmonary aspergillosis (ABPA) presents with type 1 HS reaction & asthma like symptoms.
- Aflatoxicosis is aflatoxin (hepatotoxin) mediated d/s d/to *A. flavus*.
- Otomycosis is d/s *A. niger*.
- Keratomycosis is d/s *A. fumigatus*.
- M/c fungal infection seen in immunocompetent (non-HIV) host.

Rhinocerebral Mucormycosis/ Zygomycosis

- Caused by Mucor in diabetics
- D/g : biopsy shows aseptate hyphae , ribbon like, branching at right or obtuse angle.

Candida

- M/c opportunistic infection in HIV/AIDS
- Ovoid/ spherical budding cell which produces pseudomycelia (pseudohyphae) both in culture & tissues.
- Chlamydospores⁺, germ tubes⁺, blastocyst +nt
Raynaud's Brodie phenomena⁺, jock itch, diaper rash

Histoplasma

- Uncapsulated, oval budding yeast present inside macrophage.
- Tuberculate macroconidia⁺
- Histoplasmosis is also k/as Darling d/s or Caver's d/s.

Cryptococcus

- Urease +ve encapsulated .
- True yeast (multiply by budding)
- Blastospore⁺, capsular halo⁺
- Highly pathogenic fungus in HIV +ve patient.
- Infection acquired by inhalation of soil contaminated with pigeon droppings, causes **European blastomycosis**.
- Prominent polysaccharide capsule.
- **Capsular halo is seen in India ink preparation of CSF.**

- Differs from non-pathogenic species of cryptococci by its ability to grow at 37°C and production of phenol oxidase.
- 4 serotypes A,B, C, & D . Most infections are caused by A and D

- Ubiquitous molds are filamentous fungi which form true mycelia and reproduce by sporulation (e.g. dermatophytes)
- M/c fungus producing meningitis in immunocompromised host is *Cryptococcus*
- All dimorphic fungi cause infection through respiratory infection except *Sporothrix schenckii* (thorn injury)

Diagnostic Clues

	Hyphae	Other /f	D/s
Rhizopus	Broad Non-septate	Sporangia arising from stolon	Zygomycosis
Aspergillus	Septate, branching at 45°	Common in immuno-compromised/ diabetic patient	Hyper-eosinophilia
Zygomycosis/ Mucor (Phycomycetes)	Broad 90° Non-septate	-	Rhino-cerebral mucormycosis
Candida	Pseudo-hyphae	Single budding yeast cell, Chlamydospores ⁺	-
Blastomyces	Dimorphic	Double contour, Broad based budding yeast	Infection of sinuses, North american Blastomycosis
Coccidio mycosis	Dimorphic	Non-budding yeast, arthrospores (Spherules ⁺ with endospores)	Desert rheumatism/ Valley fever by <i>C. immitis</i>
Paracoccidio mycosis	Dimorphic	Spheres with ship wheel pattern	South american Blastomycosis
Sporotrichosis	Dimorphic	Round cigar shaped budding yeast in tissue surrounded by asteroid bodies	Gardener's d/s seen in North Himachal d/to thorn injury,
Penicillium	Dimorphic	-	-

DI- Morphic Fungi

They exist in both yeast form (single celled at 37° C) and mould form (filamentous form at 25° C). Thermally di-morphic.

Dimorphic fungi	Parasitic form
Chromoblastomycosis	Muriform cells
Blastomyces dermatoidis	Yeast
Coccidiomyces immitis	Spherules
Emmonsia parva	Adiaspores
Histoplasma capsulatum	Yeast and short hyphae
Paracoccidioides brasiliense	Yeast, pseudohyphae
Penicillium marneffei	Hyphae, chlamydoconidia
Sporothrix schenckii	

POINTS OF SPECIAL MENTION

- Usually rickettsiae are not culturable, only rickettsia which is culturable --- *R. Quintana*
Among Hepatitis viruses only *HAV* can be cultured.
Among various strains of Rota virus, only *type-A* strain can be cultured.
- All *Shigella* ferment mannitol *except* *Sh. dysenteriae*.
- Lactose is not fermented by *Shigella except Sh. sonnei* and paracolon which are late lactose fermenting.
- All botulinum toxins are neurotoxic except C_2 (which is cytotoxic)
- Component of streptococci which cross reacts with the human synovial membrane --- hyaluronidase
- Maltase crosses are seen in*
- *Babesia microti* (in PBS)
- *Cryptococcus neoformans* capsule (in polarized light)
- The common mode of infection of the *Pasturella multocida* --- Animal bite
- E-coli* toxins
- LT Cholera like (acts via c-AMP)
- ST Poorly antigenic (acts via c-GMP)
- VT Shiga like toxin (SLT, cytotoxic in vero or HeLa cells)
- IL-1 is produced by all cells, IL-2 by CD_4^+ cells and IL-4,5,6 by mast cells.
- In Kala-azar there is hyper gamma-globulinemia (with pancytopenia and relative lymphocytosis/monocytosis and reversal of albumin : globulin ratio). Globulin gives +ve aldehyde test.
Other imp. conditions with Hyper γ -globulinemia - HIV, sarcoidosis, sickle cell disease.
- CI/f of infectious mononucleosis + Monospot test positive in --- EBV
Infectious mononucleosis like syndrome monospot test

negative in --- CMV.

- Diagnostic investigation : Sputum culture (Definitive) in TB
Most commonly used : Sputum examination investigation in TB (Chest X-ray in India)
Most rapid (fastest) & : Auramine rhodamine most sensitive method
- Pneumocystis Carinii* is now k/as *Pneumocystis jirovecii*
- If a bacteria acquires genes coding for restriction endonuclease, bacteria will die as it lacks methylase.

Involvement of reproductive organs in infections

D/s	Epididymitis	Orchitis	Oophoritis
Gono	+	-	
TB	+	Rare	+
Syphilis	-	+	+
Mumps	-	+	+

[Mnemonic : TestIS : Testes Involved in Syphilis]

SOME IMPORTANT NEGATIVE POINTS ASKED IN EXAMS

- In Chlamydial infection
Urethritis+, cervicitis+, salpingitis+, proctitis +, Epididymitis+. But no orchitis and vulvitis
- In Gonococcal infection
- Epididymitis+
- But no orchitis
- In TB
- Epididymitis+
- But rarely orchitis
- In Syphilis
- Orchitis+
- But no epididymitis, oophoritis
- In Mumps
- Orchitis+, Oophoritis+
- But no epididymitis, no pneumonia
- Pneumonia, appendicitis do NOT occur in --- Mumps
- Pancreatitis, aseptic meningitis do NOT occur in --- Measles
- NOT involved in cryptococcus infection --- Kidney
- Nephritis does NOT occur in --- Disseminated gonococcal infection
- Vertigo does NOT occur in --- Diphtheria

- Diarrhea is NOT seen in --- Botulism
- Fever is NOT seen in --- Botulism, staph. food poisoning.
- Viremia does NOT occur in --- Rabies
- Viral inclusions are NOT seen in --- JE, polio virus infection.
- Capsular virulence is NOT seen in --- Bordetella pertussis.
- Infant botulism is NOT caused by --- preformed toxin
- Transovarian transmission is NOT seen with --- Louse, Flea.
- NOT transmitted by lice --- Q fever
- NOT a component of Dane particle --- Delta antigen
- EBV is NOT a/w --- Laennec's cirrhosis (*NB:EBV is a/w IM, Burkitt's lymphoma & nasopharyngeal carcinoma*).
- NOT true about carbohydrate antigen --- Memory response is seen
- Staphylococci do NOT produce --- sphingomyelinase.
- HUS is NOT caused by --- Vibrio cholerae
- NOT true of scrub typhus --- Adult mite bites the vertebral host
- NOT true of congenital toxoplasmosis --- Ig G is diagnostic
- Enteroviruses do NOT cause --- Hemorrhagic fever
- Rickettsia which do NOT cause rash --- Q-fever
- Enterotoxins are NOT produced by --- Streptococcus
- Non invasive diarrhoea is NOT caused by --- B. cereus
- NOT an acid fast organism --- Mycoplasma
- Clostridial species which does NOT produce gas gangrene --- Cl. sporogenes
- NOT a saccharolytic clostridia --- Cl. sporogenes
- NOT useful in DNA analysis --- Monocytes
- NOT responsible for transmission of drug resistance --- Transposon
- Conjugation does NOT involve --- Bacteriophage
- NOT a dimorphic fungi --- Candida, Phialophora, Cryptococcus
- NOT true regarding campylobacter jejuni --- Humans are the only reservoir.
- NOT an example of superantigen --- Exfoliative toxin
- NOT a causative agent of Madura foot --- Candida
- Sputum examination is NOT useful in --- Trichinella, Babesia.
- Pulmonary eosinophilia is NOT seen --- babesiosis
- Mycobacterial species are NOT differentiated by --- oxidase test.
- Anti tubercular drug susceptibility can NOT be done by --- disc diffusion method.
- NOT a function of complement --- B-cell transformation

- NOT true of streptococcal toxin --- erythrogenic toxin is plasmid mediated
- NOT true of clostridium perfringens --- Hyluronidase is the most important toxin.
- Autoclaving is NOT suitable for --- Plastic syringes, sharp instruments.
- Diarrhoea is NOT caused by --- Picorna viruses

CLINICAL VIGNETTES

- A labourer involved with repair - work of sewers was admitted with fever, jaundice and renal failure. The most appropriate test to diagnose the infection in this patient is:

[AIPGMEE - 2003]

- A. Weil Felix test
- B. Paul Bunnell test
- C. Microscopic agglutination test
- D. Micro immunofluorescence test

(Ans: Microscopic agglutination test)

Pt in qn. is most likely suffering from Weil's d/s (leptospirosis), which is transmitted by rat's urine and manifests as ictero-hemorrhagic fever. D/g is based on MAT

- Thirty-eight children consumed eatables procured from a single source at a picnic party. twenty children developed abdominal cramps followed by vomiting and watery diarrhea 6-10 hours after the party. The most likely etiology for the outbreak is:
- A. Rotavirus Infection
 - B. Enterotoxigenic E. coli infection
 - C. Staphylococcal toxin
 - D. Clostridium perfringens infection

(Ans: Clostridium perfringens infection)

Incubation period and food items give the clue .

Clostridium perfringens manifests 8-16 hour after ingestion of contaminated food and char/by cramps and watery diarrhoea.

Staphylococcal FP may follow 2-6 hours after the ingestion of contaminated food which cooked food and milk products. It is char/by nausea, vomiting and diarrhoea within 2-6 hours of consuming food.

- A Gardner has multiple vesicles over the hand and multiple eruptions along the lymphatics. M/c fungus responsible

is ---

[AIIMS Nov'08]

- A. *Cladosporium*
- B. *Sporothrix Shenkii*
- C. *Candida*
- D. *Histoplasma*

(Ans.: B. *Sporothrix Shenkii*)

Sporothrix Shenkii causes lymphocutaneous d/s. It accounts for ~80% of cases, secondary lesions ascend along the lymphatics that drain the area, producing small painless nodules that erupt, drain, and ulcerate.

- A Girl from shimla presented to the OPD with fever, malaise, axillary and inguinal lymphadenopathy. culture shows stalactite growth. Causative organism is

[AIIMS Nov'08]

- A. *Yersinia pestis*
- B. *Pseudomonas pseudomallei*
- C. *Francisella*
- D. *Bordetella pertussis*

(Ans.: A. *Yersinia pestis*)

Clinical features of fever, malaise, axillary and inguinal lymph nodes are very much suggestive of bubonic plague, caused by *Yersenia pestis*, which was confirmed by culture showing "Stalactite growth" on ghee broth culture.

- A diabetic patient presents with bloody nasal discharge, orbital swelling pain. Periorbital pus was taken and material was sent for culture. Culture showed branching septate hyphae. Most likely organism was---

- A. *Rhizopus* B. *Aspergillus*
- C. *Mucor* D. *Candida*

[AIPGMEE 2010]

(Ans. *Aspergillus*)

- *Rhizopus/ mucor* produce broad non-septate hyphae.
- *Aspergillus* produces branching septate hyphae. Common in immunocompromised/diabetic patient
- *Candida* forms mycelia and pseudohyphae.

A middle age male presents with chest pain, fever and cough Sputum examination was negative for mycobacteria. Culture of the organism showed aerobic growth with branching pattern, slight acid fastness and gram positivity.

Most likely organism was--- [AIPGMEE 2011]

- A. *Actinomyces* B. *Aspergillus*
- C. *Nocardia* D. *Cryptococcus*

(Ans. C. *Nocardia*)

Nocardia is a filamentous, acid fast, catalase +ve, weakly staining Gram +ve, rod shaped bacteria. It can lead to slowly

progressive pneumonia.

- An elderly male presents with chest pain, fever and dry cough. Sputum culture on charcoal yeast medium revealed gram negative bacilli. Most likely organism is---

[AIIMS Nov'11]

- A. *Actinomyces* B. *Burkholderia cepacia*
- C. *Nocardia* D. *Legionella*

(Ans. D. *Legionella*)

H. influenzae is common in infancy. *Moraxella* is gram positive.

Burkholderia cepacia or *pseudomonas cepacia* is opportunistic environmental pathogen which can cause fatal necrotising pneumonia. It grows well on ordinary media. *Legionella* can cause pontiac fever and atypical pneumonia. Special media (like BCYE, or charcoal yeast medium) are required for its growth. Hence it is the answer.

- A 7 month old infant with the history of incomplete childhood vaccination presents with bouts of spasmodic cough with cyanosis and a typical inspiratory whoop. Which of the following is most appropriate clinical specimen to be collected for the isolation of pathogen.

[AIPGMEE 2011]

- A. Cough plate culture
 - B. Per oral swab
 - C. Nasopharyngeal swab
 - D. ET aspirate
- (Ans. C. Nasopharyngeal swab)

Clinical picture of infant is typical of whooping cough. Culture is considered the gold standard for the diagnosis of pertussis. Although it is 100% specific, B pertussis is a fastidious organism. Culture requires collection of an appropriate nasopharyngeal specimen obtained either by aspiration or with Dacron swab.

- A 39 yr old female presents in the emergency with headache and fever. O/e she has a neck stiffness and positive Kernig's sign. The lumbar puncture is reported as follows: Gram positive bacilli present. Most likely diagnosis is

[AIPGMEE 2011]

- A. *H. influenzae*
 - B. *Streptococcus pneumoniae*
 - C. *Neisseria meningitidis*
 - D. *Neisseria gonorrhoeae*
- (Ans. A. *H. influenzae*)

All of the above mentioned organisms can cause meningitis.

Pneumococci and Meningococci and Gonococci all are cocci. So the answer is obviously H. influenzae.

- A young male presents with urethral discharge. O/E of urine, pus cells were found but no organism was seen. Which of the following method is most suitable for the isolation of pathogen in the culture.

[AIPGMEE 2011]

- A. McCoy cell culture
 - B. Thayer Martin medium
 - C. LJ medium
 - D. Levinthal medium
- (Ans. A. McCoy cell culture)

This is a case of urethritis. M/c cause of urethritis in a young male is gonococcal infection. M/c cause of non-gonococcal urethritis is chlamydia which can produce sterile pyuria (pus in urine but no organism). Culture is the best way to isolate chlamydia. For this purpose NAAT or McCoy cell culture or HEp culture c/b used.

NOTES

CONCEPT OF HOSTS

- A *primary host or definitive host* (D/H) is a host in which the parasite reaches maturity and, if possible, reproduces sexually.
- A *reservoir host* can harbour a pathogen indefinitely with no ill effects. A single reservoir host may be reinfected several times. A reservoir host is the primary host of a pathogen.
- A *secondary host or intermediate host* (I/H) is a host that harbors the parasite only for a short transition period, during which some developmental stage is completed. For trypanosomes, humans are the secondary host, while the tsetse fly is the primary host,

Intermediate host is NOT required in

- *In most protozoans*

Like *E. histolytica*, *G. lamblia*, *Chilomastix*, *T. vaginalis*, *B. coli* (Exception are *leishmania*, *plasmodium*, *trypanosoma* which require I/H)

- *In some helminths*

Like *Enterobius*, *Trichuris*, *Ascaris*, *Ancylostoma*, *Necator*, *H. nana*

- In *T. solium* man acts as both D/H and I/H. Man is optimum host for most nematodes except
 - *Filarioidea* (I/H - Mosquito)
 - *Dracunculus* (I/H-Cyclopes)

- *Man is definitive host for most parasites except the following, in which it is an intermediate host:*

- *Plasmodium* (malaria)
- *Echinococcus granulosus* (Hydatid worm)
- *Toxoplasma*

- *Sarcocystis indonensis* [Mnemonic : PETS]

- 2 I/H are required in :

	IH ₁	IH ₂
<i>C. cinensis</i>	Fresh water snail	Cray fish
<i>P. westermani</i>	Snail	Crab
<i>D. latum</i>	Fresh water crustacean/ cyclops	fish

- *Epizootic (Amplifier or amplifying) host* is a vertebrate host in which infectious agent multiply rapidly to high level and provide source of infection to blood feeding arthropode vector. Examples are

- Arboviral encephalitis (Pigs in JE)
- House flea in plague

- *Enzootic host*

- Rodents in plague

COMMON POINT

Infective stage

Stage	Parasite
Cyst	<i>Giardia intestinalis</i>
Mature quadrinucleate cyst	<i>Entamoeba</i>
Promastigote	<i>Leishmania donovani</i>
Amastigotes	<i>Trypanosoma</i>
Cercaria	<i>Schistosoma & fasciola</i>

Parasites entering by penetration of skin

- *Ancylostoma duodenale / braziliensis*
- *Necator americanus*
- *Schistosoma*
- *Strongyloides*

Parasites transmitted by sexual contact

- *Trichomonas vaginalis*
- *Entamoeba histolytica*
- *Giardia lamblia*

Parasites transmitted congenitally

- *Toxoplasma gondii*
- *Plasmodium* spp.
- *Microsporidia*
- *Trypanosoma cruzi*

Neuroparasites are

- T. Solium,
- Acanthamoeba, Naegleria

Parasites present in muscles

	Organism		Found in m/s of
LARVA OF	Taenia saginata	Cysticercus bovis larva	Cow/buffalo
	T. solium	Cysticercus cellulose larva	Pig (pork)
	Trichinella spiralis	Encysted larva	Pig, rat, human
CYST OF	Toxoplasma	Pseudocysts	human cardiac muscles
	Echinococcus granulosus	Hydatid cyst	

- *Strongyloides*, *Necator Americans*, *Ascaris* - pass through the lung during infectious cycle in human but *Wucheria bancrofti* does not. However *Wucheria bancrofti* may cause pulmonary eosinophilia.
- Parasitic ova which is infectious as soon as passed in stool --- enterobius

PARASITIC TEST

- String test is positive with Giardia, cryptosporidium, strongyloides, Vibrio parahaemolyticus
- Skin snip is positive in - Onchocercariasis
- Sabin Feldman dye test - Toxoplasmosis
- Frenkel's skin test - Toxoplasmosis
- Xenodiagnosis - Trypanosoma cruzi (Chaga's d/s)
- Fairleys test - Schistosomiasis
- Casoni's test - Hydatid cyst.
- Montegro test - Leishmaniasis

- Epidemiologically important tests are Frenkel's skin test and Montegro test.

- Charcoat Leyden crystals are seen in
 1. Entamoeba histolytica
 2. Whipworm dysentery
 3. Ascaris pneumonia
 4. Bronchial asthma

PROTOZOANS

Cystic Stage is NOT seen in

1. Trichomonas vaginalis
2. Trichomonas intestinalis
3. Di-entamoeba fragilis
4. Entamoeba gingivalis

- Protozoan cysts are stored in → Low viscosity polyvinyl alcohol (LV -PVA).
- Infective stage in all protozoan is cyst except ---Trichomonas
- Small intestinal amoeba is --- Di-entamoeba fragilis
- Largest intestinal parasite/ largest protozoa is --- B. coli
- Only ciliate protozoan --- B. coli
- M/c protozoan parasite --- Toxoplasma gondii
- Giardia lamblia is found in jejunum & duodenum & inhibits digestion in intestinal mucosa. It does NOT invade mucosa. Limited to lumen of human SI.
- Glycogen vacuoles & chromated bodies are absent in quadrinucleate cyst of amoeba.
- Undulating membrane is seen in trichomonas & hemoflagellates.
- Pathogenicity in entamoeba is indicated by zynodene pattern
- Premunition is immunity to re-infection. Seen in syphilis, cutaneous leishmaniasis, hyper/holo-endemic malarial areas.
- Eosinophilic meningoencephalitis is caused by angiostrongylides, Gnathostoma

Primary Amoebic Meningoencephalitis (PAM)

- Causative agent : Naegleria fowleri, Hartmannella, Acanthamoeba castellanii. Balamuthia also causes amebic meningoencephalitis in immunocompromised host.
- Infection is acquired by contaminated water with trophozoites/cyst, inhalation of dust
- I.P.: 2-15 days
- Target tissue : Olfactory neuroepithelium

- *Cl/f* : Nausea, vomiting, meningismus, headache, fever, photophobia, cranial nerve palsies (III, IV, VI), seizures and coma.
- *D/g* : Wet mount of CSF shows motile trophozoites. The diagnosis of Naegleria should be considered in any patient who has purulent meningitis without evidence of bacteria on gram staining, antigen detection assay and culture.

SLEEPING SICKNESS

- Also k/as human African trypanosomiasis (HAT)
- Zoonosis caused by *T. brucei*

	West African	East African
Organism (Caused by)	<i>T.b. gambiense</i>	<i>T.b. rhodesiense</i>
Vector	<i>Glossina palpalis</i>	<i>Glossina morsitans</i>
Reservoir	Human	Antelope, cattle
Disease	Chronic	Acute
D/g by rodent inoculation	No	Yes
T/t	Pentamidine Eflornithine (stage II)	Suramin Melarsoprol (stage II)

- Lab/f: polyclonal IgM, heterophile antibodies, RF are present. Trypanomas are frequently found in CSF.
- Stages:
 - Stage I*:
Fever + ↑LN Winterbottom's sign (d/to posterior cervical lymphadenopathy) is seen.
 - Stage II*:
CNS involvement & abnormal CSF is seen. Daytime somnolence & EPS features/Parkinson's d/s may develop.
- T/t: Nifutrimox & Benznidazole

CHAGA'S D/S

- Also k/as American trypanosomiasis
- Zoonosis caused by *T. cruzi*.
- Transmitted by hematophagous tritomine insects, reduviid bugs.
- C/b transmitted by BT(blood), tissue transplant.
- Heart is m/c affected. Cardiomyopathy results in

biventricular failure.

- In GIT megadisease (**megaesophagus/megacolon**) is seen.
- D/g: Detectⁿ of motile organism in fresh blood or buffy coat. In the late stages of African trypanosomiasis, trypanosomes may be found in the CSF together with IgM - containing morula (**Mott**) cells. Mott cells are seen in the excretory part (protonephridia) of Trypanosomes.
- T/t: Nifutrimox & Benznidazole

LEISHMANIASIS

- Leishmania is obligate intracellular protozoa which resides in macrophages of RES.
- Anthroponotic/zoonotic transmission is seen.
- T_H¹ response is seen.
- Causes group of disorders. Broad categories are visceral, cutaneous, & mucosal leishmaniasis.

	Caused by	Vector
VL (kala-azar), PKDL	<i>L. donovani</i>	<i>Phlebotomus argentipes</i>
CL (oriental sore)	<i>L. tropica</i>	<i>P. sergenti</i>
CL, new world	<i>L. viannia</i>	<i>Lutzomyia</i>
CL, Diffuse	<i>L. mexicana, amazonensis, pifanoi</i>	<i>Lutzomyia</i>
ML/MCL	<i>L. braziliensis</i>	<i>Lutzomyia</i>

- Dx: In peripheral blood buffy coat is best to examine. Microscopy reveals LD bodies. For culture **NNN media**, Schneider's media is used.
- Napier's aldehyde test is also used to diagnose it.
- Antimonial compounds (sodium stibogluconate/meglumine antimonate) are DOC but resistance is seen in Bihar where AmB or miltefosine are DOC.

PROTOZOA

Order	Species	Infective form	Invasive form/Host	D/g	Pathogenicity	Remarks
Intestinal / Epithelial						
Amebae	<i>Entamoeba histolytica</i>	Cyst (4 nuclei) Contains glycogen vacuoles & chromated bodies	Trophozoite (contain no red cells & no bacteria)	IHA (m/c used), ELISA (best)	Ambic dysentery liver abscess flask shaped ulcers	Anchovy sauce pus found in abscess, aspirates are collected from edge
Ciliates	<i>Balantidium coli</i>	Cyst	Trophozoites	Trophozoites in stool (V-shaped nucleus)	Abscess & ulcer	
	<i>Toxoplasma gondii</i>	Cyst ingestion in under cooked meat or freshly passed cat's faeces	Tropho D/H domestic cat I/H - Human	Sabin feildman dye test	Disseminated infection e.g. encephalitis	Tachyzoites have predilection for parenchymal & RES
Mastigophora	<i>Giardia lamblia</i>	Cyst (not killed by chlorination)	Trophozoite is Pear shaped with tennis racket app.	String test ⁺ Acid fast	Traveler's diarrhea, Non bloody foul smelling diarrhea	A/w common variable immunodeficiency
	<i>Trichomonas Vaginalis</i>	No cyst stage	Trophozoite Pear shaped	Motility in smear	Urethritis, vaginitis (Greenish, yellow, Frothy discharge)	"Strawberry cervix" on calposcopy, fiery red vagina & Cx
Coccidia	<i>Isospora belli</i>	Cyst	Oocyst	Acid fast	Chronic enterocolitis	
	<i>Cryptosporidium</i>		Thick walled cyst	Acid fast	Chronic enterocolitis	
Free Living Amebae						
Ameboflagellate	<i>Naegleria fowleri</i>	Warm fresh water (through nose)	Tropho, cyst	motile tropho on wet mount of CSF	Primary amebic meningoencephalitis (PAM)	Acute & fatal course
	<i>Acanthamoeba</i>	Soil, water	Tropho, cyst	Tropho, cyst in biopsy	Granulomatous amebic encephalitis, keratitis	In cronically ill/ Immunosupressed pt, ICSOL
Blood stream						
Hemo-sporidia	Plasmodium sp.	Sporozoite inocula ⁿ by mosquito bite	Man is I/H		Malaria	
	Babesia	Sporozoite			Babesiosis, Piroplasmosis (In animals)	
Hemo-flagellates	Trypanosoma brucei	Metacyclic trypomastigote	Tsetse fly (Glossina)		Sleeping sickness	Winter bottom sign (d/to post cervical LN-pathy)
	Trypanosoma cruzi	Infective parasites	Reduviid bug		Chaga's disease	Romana's sign (u/L edema of eye lid)
	Leishmania donovani	Promastigotes Amastigote inside the macrophage	Bite of sandfly (Phlebotomus)	BM aspirates shows LD bodies	Kalaazar	RES is most severely affected

CESTODES

Cestode	Mode of transmission Ingestion of	I/H Host	Main site & Lesion	D/g, Rx	T/t (DOC)
<i>T. Solium</i>	Undercooked pork containing cysticercus cellulose larva	Pig	M/c site-Muscles also brain & eyes (Neuro-, ocular- cysticercosis)	Proglottis in stool,	Praziquantel / albenda (+steroids for Neurocysticerci)
<i>T. Saginata</i>	Cysticercus bovis present in raw, undercooked beef	Cattle (Cow/ Buffalo)	Intestine (jejunum)	Proglottids in stool	Praziquantel
<i>D. Latum</i>	Plerocercoid Larva of fish	Fish & copepods	Ileum	Operculated eggs in stool	Praziquantel
<i>Echinococcus granulosus</i>	Eggs in food contaminated with dog faeces	Sheep and man (D/H - Dog, wolf)	Hydatid cyst, m/c site is liver (lung in children) Calcificat ⁿ is least likely in lungs	Dx by biopsy or CT	Surgery is TOC (DOC Albendazole)
<i>H. nana</i>	Embryonated eggs Anal. oral transfer (Auto infection)	No I/H required D/H man, rat	Ileum	Egg in stool	Praziquantel

→ Niclosamide is not advised in neurocysticercosis due to risk of cyst rupture.

→ *E. multilocularis* causes : Malignant hydatid disease

→ Smallest tapeworm (cestode) is : *Echinococcus granulosus*

→ Dwarf tapeworm is : *H. nana*

→ Longest tapeworm (longest helminth also) : *T. Saginata*

→ Largest intestinal fluke/trematode : *F. buski* (giant intestinal fluke) [Remember - Buski Bada]

→ Hydatid cyst and trichuriasis are caused by ingestion of infected eggs via feco-oral route from contaminated soil

NEUROCYSTICERCOSIS (NCC)

◦ Caused by *T. Solium*.

◦ Serology :

The enzyme-linked immunoelectrotransfer blot assay (EITB) has sensitivity of 98% and specificity of 100%.

However, its sensitivity in case of single enhancing or calcified lesion is much lower. Serology should be used in conjunction with neuroimaging.

◦ MRI is better to CT as it may show scolex (eccentric spots) in the encysted lesion.

◦ D/d : Tuberculoma

In contrast to tuberculoma cysticerci are generally multiple, scolices may be visible in MRI. Eccentric dots c/b seen on CT.

An enhancing ring lesion that is <20 mm in size, regular in outline (a/w scolex) and not producing a midline shift is likely to be NCC while with tuberculomas the lesion is

usually >20 mm, irregular in outline and may produce midline shift.

◦ T/t

1. Parenchymal neurocysticercosis

Viable cysts --- Cysticidal treatment + steroids

Calcified --- AED; No cysticidal therapy .

Enhancing lesions

Single --- AED; Cysticidal drugs if persistent

Multiple --- Anticonvulsant + cysticidal and steroids

2. Extraparenchymal neurocysticercosis

Intraventricular cyst --- Neuroendoscopic removal

Subarachnoid cyst --- Cysticidal treatment + steroids, VP shunt if required

Calcified --- AED; No cysticidal t/t.

Hydrocephalus with

no viable cyst --- VP shunt, no cysticidal treatment.

3. Spinal cysticercosis --- Surgical treatment

4. Ocular cyst --- Urgent treatment

Albendazole destroys 75-90% of parenchymal brain cysts and has been superior to praziquantel in several trials comparing the cysticidal efficacy of these drugs. Corticosteroids are used as an adjunct to cysticidal therapy to control the inflammatory reaction that usually occurs 2-5 days after initiation of therapy and decrease the symptoms (headache, nausea, vomiting and seizures) caused by the death of larvae.

NEMATODES

Nematode	Mode of infection	Loca ⁿ in host	Stages & Disease	Diagnosis	T/t
<i>Enterobius vermicularis</i> (Pin or seat worm)	Ingestion of egg, Anal-oral/ self / autoinfection	LI	Female worms migrate out of anus and lays egg on perianal skin causing itching / perianal pruritus (vulvovaginitis)	Eggs on perianal skin, (NIH swab or scotch tape)	Mebendazole or pyrantel pamoate
<i>Trichuris trichura</i> (Whipworm)	Ingestion of egg from feces, contaminated soil	LI	Worm in colon may cause rectal prolapse	Barrel shaped eggs in stool	Mebendazole
<i>Ascaris lumbricoides</i> (Round worm)	Eating viable eggs from feces	SI	Loeffler's pneumonia d/ to migration through lungs	Oval egg with irregular surfaces	Mebendazole (Pyrantel pamoate in pregnancy)
<i>Ancylostoma duodenale</i> <i>Necator Americans</i> (Hook worms)	Filariform larva <u>penetrates skin</u>	SI	Worms in colon causes blood loss leading to anemia	Eggs or Rhaditiform filiiform larva in stool	Mebendazole
<i>Strongyloides stercoralis</i>	Filariform larva <u>penetrates skin</u> or through autoinfection	SI ,lungs	Eosinophilia, <i>hyperinfection</i>	Larva in stools and eggs also	Ivermectin
<i>Trichinella spiralis</i>	Larva in under cooked meat esp. pig.	M/s	Encysted larva in human m/s causing myalgia; subconjunctival h'age, periorbital oedema	Encysted larva in human m/s and serology	Mebendazole, steroids
<i>Ancylostoma</i> (Cutaneous larva migrans)	Contact with soil contaminated with dog and cat feces	S/c,	Migrating larva in S/c tissue → creeping eruption (cutaneous larva migrans), Ground itch	Clinical	Thiabendazole Albendazole
<i>Dracunculus medinensis</i> (Guinea worm)	Drinking water with cyclops containing larva	S/c	Female worms → Skin blisters usually in leg/ foot	Clinical head of female worms appears through ulcer	Thiabendazole
<i>Toxocara canis</i> (Visceral larva migrans)	Ingestion of eggs in dog and cat feces	Lung, liver, eye, brain	Larva migrates in viscerae (Blindness), Visceral & ocular larva migrans	Clinical or serological	Albendazole and DEC

- Ground itch / *Ancylostoma dermatitis* - is caused by *Necator*
- Cutaneous larva migrans / cutis and creeping eruptions are caused by --- *Ancylostoma braziliense* & *A. caninum* (T/t Thiabendazole)
- Visceral Larva migrans is caused by --- *Toxocara cani*
- Ocular larva migrans is also caused by --- *Toxocara cani*
- Larva currans - by *strongyloides* (also Hyperinfection syndrome, auto infection)
- *Toxocara canis* belong to gonchorist/ unisexual parasite.
- Loeffler syndrome is --- D/to *Ascaris*
- Largest nematode --- *Placentonema gigantisma* > *Ascaris*
- Smallest nematode --- *Trichinella*

• Mode of infection of Nematodes

1. Ingestion of eggs :-

Enterobius,

Ascaris,

Trichuris

[Mnemonic : EAT]

2. Ingestion of larva within I/H --- *Dracunculus*3. Ingestion of encysted larva in m/s --- *Trichinella*4. Skin penetraⁿ --- *Strongyloides*, *Ancylostoma*, *Necator*5. Blood sucking insects --- *Filariae*6. Soil/dust --- *Enterobius*, *ascaris*

Among Nematodes

	Examples	Remark
Oviparous (HEAT)	Hookworm (Ancylostoma/ Necator)	Segmented eggs
	Enterobius	Eggs containing larva
	Ascaris, Trichuris	Unsegmented eggs
Ovo-viviparous	Strongyloides stercoralis	
Viviparous (Producing larvae)	Wucheria bancrofti, Trichinella, Brugia malayi	

Larva in Stool

- Strongyloides
- Hookworm (Filiform larva)

Autoinfection is seen in

C = Capillariasis

S = Strongyloides

E = Enterobius

T = Taenia solium

H = H. nana

[Mn: Chhotu SETH]

- Nematodes that crawl out : Enterobius, T.saginata

Eggs do not float in saturated NaCl solution

T. solium / saginata

Unfertilized eggs of Ascaris

Intestinal flukes [mnemonic-Suit]

Eggs in Stool

- Bile stained (coloured) : Ascaris, Trichuris
- Non-stained (colourless) : Hookworm, Enterobius, H. nana
[Colored BAT & colorless HEN]

TREMATODES

- Blood flukes are transmitted by skin penetration by cercariae released from snails. Rest all other flukes are transmitted by ingestion of metacercariae.
- S. Japonicum causes -Katayama disease, cirrhosis of liver
- S. mansoni causes - pipestem (periportal) cirrhosis.
- C. sinensis causes biliary obstruction, cholangiocarcinoma.
- Largest trematode infecting man --- F.buski

IMP. TREMATODES (FLUKES)

Trematode	Also k/as	Inhabitat of	Transmitted by	I/H	Features	D/g	T/t
Schistosoma Japonicum	Oriental blood fluke	SMV plexus	Skin penetra ⁿ (free cercarials)	Snail	Small lateral spine (Knobs)		Praziquantel
S. Mansoni		IMV plexus	Skin penetra ⁿ	Snail	Large lateral spine		Praziquantel
S. Hematobium		Vesical plexus	Skin penetra ⁿ	Snail	Large terminal spine		Praziquantel
Clonorchis Sinensis	Oriental liver fluke	Liver	Ingested with raw crabs	Snail / Cray fish	Operculated Eggs		Praziquantel
Paragonimus Westerni	Oriental lung fluke	Lung	Ingested with raw crabs	Snail & crab	Operculated	Based on demonstration of eggs in sputum & stool	Praziquantel
Fasciola Hepatica		Liver	Ingestion of water with metacerceria	Snail	Egg in stool		Triclabendazole Bithionol

IMP. NEGATIVE POINTS

- Malabsorption syndrome is NOT a/w --- Ascaris
- Cystic stage is NOT seen in --- Trichomonas vaginalis
- Parasite which do NOT produce neurological manifestation --- Trichinella spiralis
- Parasite which do NOT produce biliary obstruction --- Girardia
- Malabsorption syndrome is usually NOT seen with --- Ascaris lumbricoides
- NOT commonly seen in Ascariasis---Anemia .
- Amoebiasis is NOT transmitted by --- Vertical transmission.

CLINICAL VIGNETTES

- A 30 year old patient presented with features of acute meningoencephalitis in the casualty. His CSF on wet mount microscopy revealed motile unicellular micro-organisms. The most likely organism is : [AIIMS May '05]

A. *Naegleria fowleri*. B. *Acanthamoeba castellanii*
 C. *Entamoeba histolytica*. D. *Trypanosoma cruzi*
 (Ans: *Naegleria fowleri*)

Acute symptoms are more common with *Naegleria* than *Acanthamoeba*. Both of which are free living unicellular amoebae

- A traveller presents with direct hyperbilirubinemia. USG abdomen was done, which revealed eggs in his biliary tract. Most likely organism is

[AIIMS May '09]

A. *Fasciola buski* B. *Gnathostoma*
 C. *Clonorchis sinensis* D. *Ascaris lumbricoides*
 (Ans: C. *Clonorchis sinensis*)

C. sinensis is also k/as oriental liver fluke. Organism enters the body by ingestion of raw freshwater fish harboring metacercariae. On reaching duodenum organism excyst and worms ascends in biliary tree where they release operculated eggs. Repeated infection may produce bile duct obstruction (direct hyperbilirubinemia is characteristic of obstructive jaundice), cholangitis or cholangiocarcinoma

- A 25 year old male presents with the recurrent episodes of watery diarrhoea for the past 6 months. Stool examination

reveals acid fast structures approximately 12 µm in diameter. the most likely etiological agent is

[AIIMS May '09]

A. *Cryptosporidium* B. *Isospora*
 C. *Cyclospora* D. *Microsporidia*
 (Ans: A. *Cryptosporidium*)

1. Chronic diarrhoea --- C/b caused by any of the above
2. Acid fast organism --- are *Cryptosporidium* and *Isospora*
3. Size 12 µm

Cryptosporidium is an acid fast, coccidian parasite. On stool examination excreted oocysts are small ~ 5-10 µm in diameter

Isospora is also an acid fast organism. On stool examination excreted oocysts are large ~25µm in diameter.

Microsporidia are small 2- 4µm, gram +ve organism.

- A child presents with diarrhoea since 1 year. The stool examination shows eggs measuring 100 microns in length. Probable organism can be all except:

[AIIMS Nov'09]

A. *Fasciola gigantica* B. *Gastrodiscoides hominis*
 C. *Opisthorchis viverrini* D. *Schistosoma mansoni*
 (Ans. *Opisthorchis viverrini*)

NOTES

LAB. VALUES WITH AGE

Parameter	Do not change with ↑ing age	Do change with age
1. LFT	S bilirubin, AST, ALT, γ -GT, Coagulation tests	ALP \uparrow
2. RFT	Serum creatinine	Cr-clearance \downarrow (GFR)
3. TFT	T_4	TSH \uparrow T_3 \downarrow
4. CBC	Hematocrit, Hb, RBC index, platelets	WBC count \downarrow
5. ABG	pH, $PaCO_2$	$\downarrow PaO_2$, $\downarrow VC$, Systolic BP, $\uparrow PP$, $\uparrow RV$
6. Biochemical	S.electrolytes Ca^{++} , Phosphate, Total protein, folate	Albumin, B_{12} , HDL, Mg^{++} in male \uparrow \uparrow Uric A., total cholesterol, HDL in female Blood glucose \uparrow

Normal Serum Values

Serum substance	Normal range
Na^+	136- 145 mEq/L
K^+	3.5 - 5 mEq/L
Ca^{++}	9-11 mg% 2.2-2.6 mmol/L
Ionic Ca^{++}	4.5 - 5.1 mg%
Cl^-	98 - 106 meq/L
Mg	1.6 - 2.1 mg%
P	2.5 - 3.1 mg%
HCO_3^-	21-24 mEq/L
Osmolality	285- 295 mmol/kg
Urea	15- 50 mg%

URINE ANALYSIS

- Thymol/ conc. HCl is used as preservative
- Normal composition

S.g. = 1.015-1.025 (but range is 1.008-1.030)
 pH, reaction = 5.0-7.0 (average 6.0), acidic
 Creatinine = 0.8-1.8 gm/L
 Urea = 25-30 gm/L
 Uric acid = 0.5 gm/L

- Normal urine output is 1-2 ml / kg / hr. (Volume = 1200-1500ml/24 hr). *Polyuria is > 3000 ml / 24 hr.*
- Abnormal constituents of urine are Ketones, albumin, glucose.

Specific gravity

- Urine of low s.g. (< 1.007) is k/as hyposthenuria & urine of fixed s.g. 1.010 is k/as isosthenuria (seen in late stages of chronic GN).
- Urinary s.g. after fluid restriction of 12 hrs. > 1.025
 Urinary s.g. after fluid restriction of 24 hrs. \geq 1.026
 S.g. after deliberate water intake of 12 hrs. \leq 1.003

Causes of

High Specific gravity	Low Specific gravity
1. Excess sweating	1. Excess water intake
2. Glycosuria	2. DI
3. Albuminuria	3. Chronic nephritis
4. Acute nephritis	(All causes of polyuria except DM)
(Causes of oliguria/concentrated urine)	

Colour of urine

Colour	Cause (due to)	Seen in
Dark yellow	\uparrow urochrome	Fever, thyrotoxicosis, starvation
Pale, colourless	\uparrow fluid intake	
Red	Hb, Mb, porphyrin, RBCs (Rmp, phenindione, Beet)	
Brownish black (dark brown on standing/ O_2)	Homogentisic acid, melanin met-Hb	Alkaptonuria ochronosis
Reddish purple on standing/ O_2	Porphyrins	Porphyria
Pinkish brown on standing (yellow brown)	Bilirubin	Hemolytic anemia

- Smoky (Cola Coloured) urine is d/ to RBCs in urine and is seen in acute glomerulonephritis.
- Reddish brown urine is d/ to free Hb or Met-Hb and O-toluidine test is +ve.

Urine sample collection

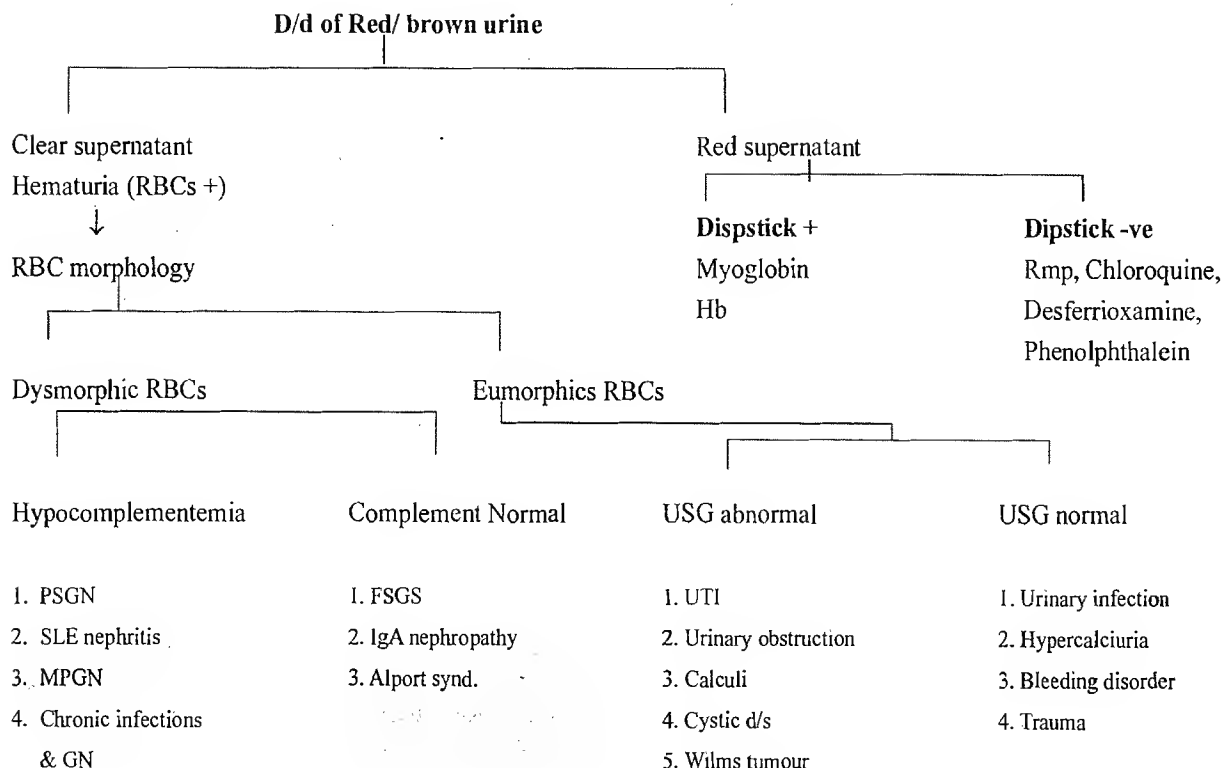
- Early morning urine sample is used for *diagnosis of pregnancy* (β -hCG based), nephrotic/nephritic syndrome
- Culture of 3 morning urine samples is required for definitive diagnosis of genitourinary TB.
- Mid stream urine sample** is required for diagnosis of UTI.
- Freshly catheterized urine sample** is required for cytologic diagnostic purpose.
- Suprapubic urine sample is best for culture sensitivity in infants for d/g of UTI.

- When the colony count is $> 10^5$ /hpf/ CFU/ mm³ of urine in a culture, it suggest bacteriuria.
- Most appropriate method for obtaining a urine specimen for culture in female infant is clean catch void sample.

HEMATURIA

There is a long list of causes of glomerular and extra glomerular hematuria. Summarized approach to hematuria is given here.

Gross		Microscopic
Visible to naked eye		Detected only by dipstick or microscopic examination
If originates from		defined as
Kidney	Lower UT and UB	> 5 RBCs/hpf (in 10 ml fresh centrifuged urine) or > 20 RBCs / hpf (In uncentrifuged urine)
↓	↓	
Brown/cola colored	pink/red colored	
Contains RBC casts	contain clots	
Glomerular diseases	Extra glomerular disease	
- IgA nephropathy	- Tubulointerstitial nephritis	
- Alport syndrome	- ATN	
- Acute nephritic syndrome	- Papillary necrosis	
- GPS	- Hemoglobinopathy	
- SLE nephritis	- Urolithiasis	
- Post streptococcal GN		
- <u>Thin GBM disease</u>		



- Glomerular hematuria is c/by **dysmorphic RBCs** in urine when examined by phase contrast microscopy as the RBC passes down through renal tubules it loses its shape and size and becomes dysmorphic.
- Non-glomerular hematuria is c/by isomorphic or **Eumorphic RBCs (>85%) & RBCs clumps but no casts** in urine. Stones, hypercaciuria, tumours are important causes.

Significance of hematuria

Presentation	Significance / Interpretation
Gross hematuria	Post renal source (in urinary tract)
Isolated hematuria	Idiopathic congenital anomaly (Alport Syndrome, PKD)
Isolated microscopic hematuria	Glomerular d/s (IgA nephropathy, hereditary nephritis, thin GBM d/s)
Hematuria with dysmorphic RBCs + RBCs casts, proteinuria > 500 mg/d	Acute GN
Hematuria + pulmonary h'age	Good Pasture syndrome (Anti-GBM d/s)

Recurrent Hematuria

Presentation	Significance / Interpretation
Sensorineural deafness + Lenticonus	Alport's
Pharyngitis f/b hematuria within 24 hr	IgA nephropathy
Wt loss, fever, RVT in middle age	RCC
Chronic analgesic use + colicky pain	Analgesic nephropathy
Renal failure	ADPKD
Colicky pain	Stone

- Alport syndrome can occur within 1st yr of life. IgA nephropathy after the age of 10 yrs & ADPKD after 3-4th decade.
- Electron microscopy is diagnostic in --- Alport's
- Solid tissue tumours in which fever is seen --- Ewing's, RCC, HCC.

Recurrent gross hematuria is seen in

- Alport's syndrome
- Berger's disease (IgA nephropathy)
- Idiopathic familial hypercalciuria
- Thin GBM d/s
- Stones (Urolithiasis)

Myoglobulinuria

- Seen after vigorous exercise.
- Pink/reddish urine, occasional amorphous debris 3-4 granular casts but no RBCs
- Myoglobin in urine is detected by **orthotoludine** reagent

Hemoglobinuria

- Seen in mismatched blood transfusion, hemolytic anemias, snake bite, copper sulphate poisoning etc.
- A/w hemoglobinemia or methemoglobinemia.

Albuminuria

- Excretion <30 mg/d → Normal
- 30- 300 mg/d → Microalbuminuria
- 300 mg - 3 g /d → Sub nephrotic proteinuria
- >3 g /d → Nephrotic range (massive) proteinuria

URINARY CASTS

- Cast is particles which precipitate in tubules in ascending limb of Loop of Henle.
- Tom Horsfall protein (THP) is a normal constituent of urine. Lack of water/ dehydration results in precipitation of THP.

Cast	Constituent	Significance/Seen in
Transparent/ Hyaline casts (Benign)	Tom Horsfall protein (THP) only	Prerenal failure, Does not represent any damage to tubules, Normally seen after strenuous exercise
Broad/waxy casts (Size ↑)	THP only	Stasis in collecting duct (CRF)
Coarse granular/ Muddy brown	THP + epithelial cell debris	ATN (Intrinsic renal tubular d/s)
WBC cast	THP + WBCs	Acute pyelonephritis
RBC casts	THP + RBCs	Acute GN
Lipid casts	THP + cholesterol	Nephrotic syndrome
Eosinophilic casts	THP + Eosinophils	Acute interstitial nephritis, Atheroembolism

- If WBCs or pus cells (not casts) are seen in urine they indicate urethritis, cystitis (not of renal origin).
- Dysmorphic RBCs in urine indicate glomerular pathology.
- Coarse granular casts in urine are always pathological.

CSF ANALYSIS

CSF Findings in important CNS disorders

Type of meningitis	Color	Opening pressure (mm water)	Cell/mL	Predominant cells	Protein (mg%)	Glucose (mg%)	Remark
Normal	Clear colourless	70-180	0-5	Lympho	15-35	45-80	Cl ⁻ 700-760 mg%
Pyogenic/ Acute bacterial	Turbid/ purulent	↑↑ (>180)	200-20,000	PMNs > 95%	↑↑ (>50)	↓↓ (<45)	↓ Cl ⁻ < 680
Aseptic/ Acute viral	clear	↑ (>250)	25-2,000	Lympho	↑ (>50)	N, ↓	
Meningo-encephalitis	Clear			Lympho			
Tubercular/ TBM	clear/ slight turbid	↑ (>300)	100-1,000	Lympho	↑ (>50)	↓ (<45)	↓ Cl ⁻ Cob web +ve
Spirochetal (Syphilitic, Lyme's d/s)	clear/ turbid	N, ↑	100-500	Lympho	↑ (25-60)	N	650-720
Meninism in acute fever	clear	N	Slight ↑ (lympho)		15-50	N	N

- In acute/early stage of TBM polymorphs may predominate.
- CSF glucose must be considered in relation to blood glucose only normally CSF glucose is 2/3rd of blood glucose (or 20-30 mg% lower than blood glucose).
- ↓ in CSF chlorides is seen in TBM
- For cryptococcal meningitis helpful diagnostic aid is antigen detection in CSF and India ink/wet mount preparation showing budding yeast.

- Average volume of CSF is 150 ml in adults, 50ml in infants (& of spinal CSF is 75 ml). Recycling rate is 3.7 times/d.
- Rate of CSF production 550 ml/d (20 ml/hr).
- In CSF there are high Mg^{++} , HCO_3^- , Pco_2 , Creatinine, Cl^- (than blood) i.e. 4 "C" and magnesium.
- CSF : plasma glucose ratio is 2:3. CSF Glucose is 2/3rd (66 %) of blood glucose.
- Absorbed by arachnoid villi through their tight junctions of their endothelium. Most CSF is extraventricular.
- CSF is absorbed by lymphatics around CN 1, 2, 7, 8
- Lumbar CSF pressure 70-180 mm CSF or 70-180 mm of water (3-12 mmHg). CSF pressure is mainly regulated by CSF absorption.
- pH of CSF - 7.33 (plasma 7.40).

Eosinophilic Meningitis

CSF shows predominance of eosinophils and mononuclear cells. It is caused by

- Gnathostoma
- Angiostrongylus cantonensis
- Baylisascaris
- Low CSF proteins may be seen in :
 - Pseudotumour cerebri
 - Recurrent LP (lumbar puncture)
 - Infants
- High CSF proteins may be seen in :
 - Infections
 - GBS
 - Multiple sclerosis
 - Malignancies
 - ICH (Intracranial H'age)
- Albumino-cytological Dissociation : Proteins increased but cells are low . A disproportionate ↑ in proteins compared to cells seen in
 - Spinal tumours
 - GBS
 - Cerebral arteriosclerosis, infarcts,
 - Multiple sclerosis

◦ **Neighbourhood reaction**

CSF shows variably ↑ed cells, normal glucose, N to ↑ proteins and variable opening pressure. Seen in mastoiditis, brain abscess, epidural abscess, sinusitis, septic thrombus, brain tumour.

Froin Syndrome

Is triad of CSF proteins > 500 mg% + xanthochromia + spontaneous clotting.

Usually there is complete spinal block d/ to tumour.

Pandy's Test

- Detects ↑ globulin in CSF (+ve in pyomeningitis),
- Disproportionately greater ↑ in gammaglobulins is seen in multiple sclerosis and in neurosyphilis
- In meningococcal meningitis ↑ in IgM and in multiple-sclerosis ↑ IgG
- Very high CSF proteins (~ 10 g/L) are most likely d/to CSF below a spinal block (usually d/ to spinal tumours)

Fibrin clots in CSF

- In pathological hemorrhagic CSF
- On standing when proteins ↑↑ (> 2g/L)
- In TBM (Cob-web like coagulum on overnight standing)
- In neurosyphilis and polio-meningitis.

Mollaret Meningitis

- Also k/as recurrent lymphocytic meningitis
- HSV is the m/c cause.
- D/g: HSV antibodies in CSF or persistence of HSV- DNA in CSF

Common Organisms in Meningitis

- Neonatal ---in India **E.coli**, **Klebsiella** spp., **Enterobacter** spp., **Proteus** spp. In west GBS are m/c
- In infants --- **Hib**(in India), **Streptococcus agalactiae**, **Listeria**.
- In children --- **Hib**(in India), **N. meningitidis**, **S. pneumoniae**
- Adolescents --- **Neisseria meningitidis**
- Adults --- **S. pneumoniae**
- Elderly --- Gram-negative bacilli
- In HIV --- **Cryptococcus**
- M/c cause of aseptic meningitis --- **ECHO** viruses

→ M/c cause of viral meningitis—**Enteroviruses**

→ M/c cause of viral encephalitis—**HSV-1**, **Arbovirus** in epidemic setting (Note: HSV-2 does not cause encephalitis)

Correction of hyponatremia in ARF

(when Na^+ fall < 120 mEq/L it may be corrected using NS or hypertonic 3% saline). Dose is calculated as

$$\text{Na (mEq)} = 0.6 \times \text{wt (kg)} \times (125 - \text{S.Na}^+)$$

- For blood glucose estimation in laboratory, fluoride is added to the blood to prevent glycolysis by cells. Fluorides inhibit enolase enzyme and thus glycolysis.

Partial pressure of oxygen in arterial blood (PaO_2)

- Partial pressure of oxygen in arterial blood by following formula.

$$\text{PaO}_2 = 104 - [\text{patient's age} \times 0.42 \text{ (in supine position)} \text{ or } \text{patient's age} \times 0.27 \text{ (in sitting position)}]$$

- So in a 85 years old healthy male PaO_2 will approx. 80 mmHg.
- PaO_2 (in supine) - 90 mmHg (at age 20 year), 82 mmHg (at 60 year) & 72 mmHg (>60 year)
- Calculation of intrinsic heart rate (IHR)
 $\text{IHR} = 118.1 - (\text{Age} \times 0.57)$

PLASMA ENZYMES

Functional Plasma Enzymes

- Are enzymes, proenzymes, or their substrates which are present all the time in blood circulation and perform physiologic function.
- They include lipoprotein lipase, pseudocholinesterase, & the proenzymes of coagulation and blood clot dissolution. The majority of these enzymes are synthesized in and secreted by the liver.

Principal Serum plasma enzymes used in clinical Diagnosis.

Serum Enzymes	Major Diagnostic Use
◦ AST (SGOT)	MI
◦ ALT (SGPT)	Viral hepatitis
◦ Amylase, lipase	Acute pancreatitis
◦ Phosphatase, acid	Metastatic cancer prostate
◦ Phosphatase, alkaline	Bone d/s, obstructive liver d/s

Isoenzymes and isoforms

	Isoenzymes	Isoforms	Found in	↑ in
LDH	LDH-1	HHHH	Heart	MI
	LDH-2	HHHM		
	LDH-3	HHMM		
	LDH-4	HMMM		
	LDH-5	MMMM	Liver	
CPK	CPK-1	CPK - BB	Brain	
	CPK-2	CPK-MB	Myocardium	
	CPK-3	CPK-MM	Skeletal muscles	

- LDH has 5 isoforms.

- Metabolic acidosis with fully compensated chronic respiratory alkalosis occurs in single condition — very high altitude.
- Met. alkalosis is most dangerous of all acid base disorders, as it may induce cardiac arrhythmias.
- Conditions where respiratory alkalosis and metabolic alkalosis both exist together are — Pulmonary embolism + diuretics
- Conditions a/w metabolic acidosis with chronic respiratory acidosis — Very high altitude
- In salicylate poisoning there is respiratory alkalosis first + ↑ salicylate anions f/b metabolic acidosis

Apply 3 simple & basic principles given below to solve any acid base query

Simple disorder

In simple acid base disorder pCO_2 and HCO_3^- levels change in the same direction.

Simple disorder	pH	pCO_2	HCO_3^-
Metabolic acidosis	↓	↓	↓
Metabolic alkalosis	↑	↑	↑
Respiratory acidosis	↓	↑	↑ (1 meq/ dL ↓ acute & 4 meq/ dL ↑ chronic)
Respiratory alkalosis	↑	↓	↓ (2 meq/ dL ↓ chronic)

ACID BASE DISTURBANCES

HCO_3^-	= 24 ± 2 mEq/L
PCO_2	= 40 ± 5 mmHg
CO_2	= 1.2 mEq/L
Base acid ratio	= 20 : 1
pH	= 7.4 (range 7.38-7.44)
Base excess	= ± 2

- pH, PO_2 and PCO_2 are measured values and HCO_3^- is calculated value.
- Change in HCO_3^- level < 15 meq/L is always associated with mixed acid base disturbance
- In fully compensated phase --- arterial pH is brought into the normal range.

The Mixed Disturbance

- If a patient with respiratory insufficiency develops metabolic acidosis, he loses his ability to compensate and a mixed respiratory-metabolic acidosis supervenes. Correspondingly, a mixed respiratory-metabolic alkalosis is also possible.
- In mixed disturbances, both metabolic (bicarbonate) and respiratory (pCO_2) factors pull in the opp. direction and pH changes are exaggerated (double arrows).

	pH	Bicarbonate	PCO_2
Mixed			
Acidosis	↓↓	↓	↑
Alkalosis	↑↑	↑	↓

Compensation for Acid - Base imbalances

- Compensation is done by an organ not primarily affected; for example, pulmonary disturbances resulting in respiratory acidosis or alkalosis will lead to compensation by the kidney. Conversely, primary disturbances of renal

function or metabolism with acid-base imbalance lead to compensation by the lungs.

- Compensation will return the abnormal pH towards normal.

PH Bicarbonate PCO_2 Compensation*

Respiratory

Acidosis	↓	↑↑	↑	
Alkalosis	↑	↓↓	↓	Renal effect on bicarbonate

Metabolic

Acidosis	↓	↓	↓↓	
Alkalosis	↑	↑	↑↑	Respiratory effect on CO_2 .

- Double arrows show direction of compensation. The pH change will be less pronounced in the presence of compensatory mechanism than in their absence.

Expected compensation

- For acute rise in PaCO_2 over 40 mm Hg, HCO_3^- increases by 1 meq/L for each 10 mmHg PaCO_2 . For each 10 mmHg PaCO_2 elevation there is ↓ in pH by .08 (example ---if PaCO_2 becomes 60 mm Hg, HCO_3^- values are likely to be 26 meq/L and pH 7.24)
- For acute fall in PaCO_2 below 40 mm Hg, HCO_3^- falls by 2 meq/L for each 10 mmHg PaCO_2 fall
- For chronic elevation in PaCO_2 over 40 mm Hg, HCO_3^- increases by 4 meq/L for each 10 mmHg PaCO_2 fall

Anion gap (AG):

In certain mixed disorders pH, PaCO_2 and HCO_3^- are normal and the only clue to an acid base disorder may be an increased anion gap. So AG is called "foot print" of metabolic acidosis. Hyperchloremic metabolic acidosis leaves no "foot print".

- (d) Compare fall in HCO_3^- with increase in plasma anion gap.

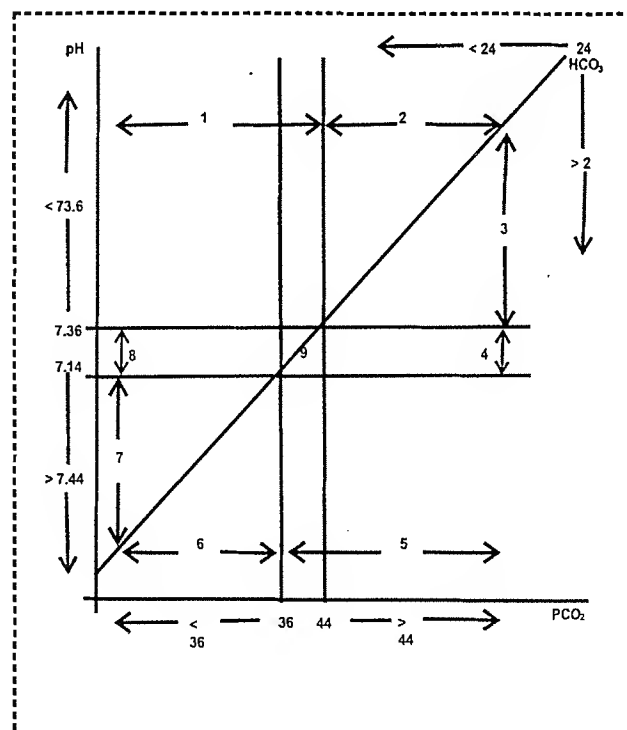
- In high AG metabolic acidosis, rise in the plasma AG (AG -12) matches with fall in serum HCO_3^- ($24 - \text{HCO}_3^-$ (24 - HCO_3^-), (Rise in AG = Fall in HCO_3^-).
- If increase in AG exceeds the fall in HCO_3^- (Rise in AG > Fall in HCO_3^-), it suggests co-existing metabolic alkalosis.
- If increase in AG is lesser than the fall of HCO_3^- (Rise in AG < Fall in HCO_3^-), it suggest loss of

HCO_3^- (diarrhoea) causing non-AG metabolic acidosis.

ABG Nomogram

The steps in using the nomogram are:

- Is the pH normal or <7.36 or > 7.44?
- Then is pCO_2 normal or <36 or >44 mmHg? Depending on the area it falls the interpretation is done as shown in Figure.
- If the values fall in area 2,3,6 & 7 see if HCO_3^- is <24 or >24. If the HCO_3^- value is between 22 - 26 the results are always isolated respiratory disturbance.

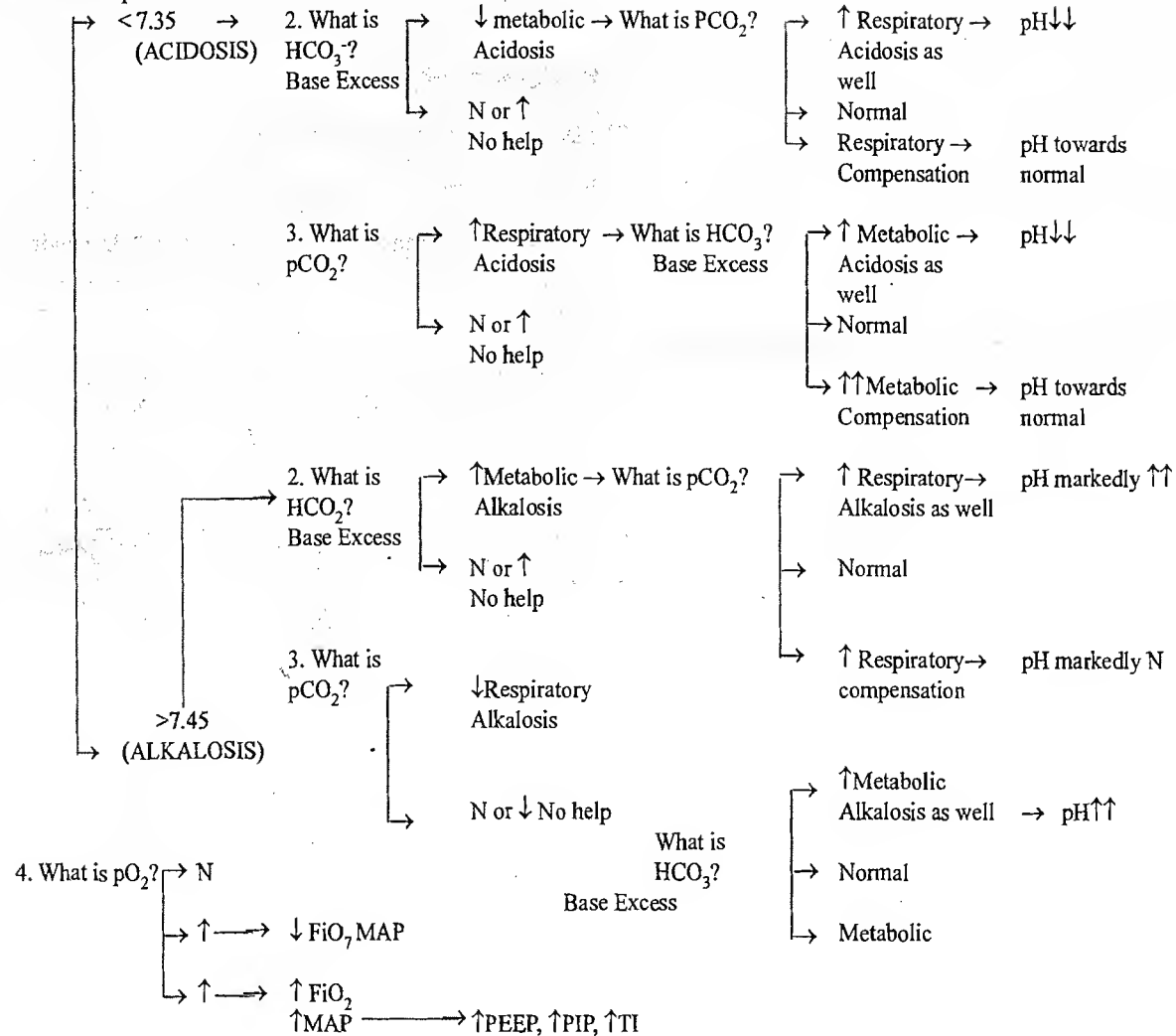


- Metabolic acidosis
- Metabolic and Respiratory acidosis
- Respiratory acidosis
- Respiratory acidosis and Metabolic alkalosis
- Metabolic alkalosis
- Metabolic and Respiratory alkalosis
- Respiratory alkalosis
- Respiratory alkalosis and Metabolic acidosis
- Normal

(Courtesy --- Dr. So. Shivbalan, Dr. P. Rajkumar, Indian Pediatrics, Vol. 42, 2005)

ABG decision tree

1. What the pH?



Some basic stains in histopathology

Stain	Used for
Hematoxylin	Nuclei, nucleoli, bacterium, Ca^{++}
Eosin	Cytoplasm, collagen, fibrin, RBCs, thyroid colloid
Oil red O	Alveolar macrophages/ dust cells, fat
Trichome	Collagen
Reticulin	Reticular fibres in loose conn. tissues
Congo red	Amyloid
PAS	Glycogen, glycoprotein, mucin, mucoprotein

HISTOPATHOLOGY

- Fixatives most commonly used in histopathology is formaldehyde (10% formalin).
- In a pap smear slide ethanol (95%) is used as a fixative to prevent air drying.
- Cytokeratin is the most important immunohistochemical stain to establish the diagnosis of poorly differentiated carcinomas.

Other important immunohistochemical stains are

Stain	Used for
Cytokeratin	Epithelial cells (Carcinomas)
Vimentin	Connective tissue
Desmin	M/s (mesenchymal tumours)
S100, NSE, neurofilaments	Neurons (Neural crest derived tumours)
GFAP	Glial cells

EXFOLIATIVE CYTOLOGY

- Useful in diagnosis of tumours which shed off tumour cells in the lumen of vicinity.
- Useful in :
 - Ca cervix
 - Ca stomach
 - Ca lung/bronchus.
 - Urothelial tumours
- BAL(bronchoalveolar lavage) is a method of aspiration of exfoliated cells in case of ca lung.

KFT (KIDNEY FUNCTION TEST)

Pre-renal azotemia

- Urinary Na^+ is $<10 \text{ m mol/L}$ & SG is >1.018
 - Fe Na $<1\%$, Renal failure index <1
 - Plasma BUN / Cr ratio $= >20$, U cr: Pl cr >40
- A disproportionate elevation of blood urea as compared to serum creatinine occurs in pre-renal azotemia
- A definitive diagnosis of CRF can be established on the basis of bilaterally reduced renal size

ASCITIC FLUID ANALYSIS

Diagnosis of spontaneous bacterial peritonitis (SBP) is made when the ascitic fluid neutrophil count is $>250/\text{mm}^3$

Cirrhotic ascitis is char/by--- Straw color, albumin $<2.5\%$, SG <1016 , WBC $<200/\text{mm}^3$

SYNOVIAL FLUID ANALYSIS

- Normal synovial fluid is clear or pale straw and is viscous, primarily because of high levels of hyaluronic acid
- Non- inflammatory SF is ---clear , viscous, and amber coloured with TLC $<2000/\mu\text{L}$ and predominance of mononuclear cells
- Joint effusions in OA and trauma have normal viscosity
- Inflammatory SF is ---turbid/ yellow, low viscosity, and amber coloured with TLC $>2000/\mu\text{L}$ and predominance of polymorphs.
- Synovial fluid of low viscosity (thin) is seen in-- Inflammatory arthritis (Gout, septic arthritis, TB, RA)
- Monosodium urate crystals are seen in gout & are long, needle shaped, negatively birefringent, intracellular
- CPPD crystals, seen in *pseudogout* and chondrocalcinosis are short, rhomboid-shaped, positively birefringent.

SPUTUM EXAMINATION

- Sputum expectoration specimen is collected for examination in
 - Mycobacteria
 - Legionella
 - Pneumocystis.
- Sputum can NOT be disinfected by chlorhexidine.

PLEURAL FLUID ANALYSIS

- Anchovy sauce appearance of pleural fluid may be seen in *Entamoeba histolytica* infection.
- Parapneumonic effusions are a/w bacterial pneumonia, lung abscess, or bronchiectasis and are probably the m/c cause of exudative pleural effusion.
- Exudative pleural effusions meet at least one of the following criteria
 - P/S protein >0.5
 - P/S LDH >0.6
 - Pleural fluid LDH $>2/3$ normal upper limit for serum
 leading causes of exudative effusions are --- bacterial/ viral pneumonias, malignancy, pulmonary embolism
- A pleural fluid NT pro BNP $>1500 \text{ pg/mL}$ is virtually diagnostic of an effusion secondary to CHF.

SEMINAL FLUID ANALYSIS

- Normal quantity of seminal fluid in a single emission is 2-6 ml and contains about 60-150 million sperms per ml, of which 90% are motile at the time of ejaculation. Analysis should be performed within an hr of collection.
- Fluid is alkaline with a pH of 7.4
- 3 Azoospermic or oligospermic results should be evaluated by chromosomal study and testicular biopsy.
- Sperm production per day - 120 million /day

Interpretation of results: (2010 guidelines)

- **Normal:**
 - Normal counts >15 million/ml
 - Quantity >1.5 ml
 - Motility >32% mobile
 - Morphology >4% normal morphology
 - WBCs <1 million/ml
 - Immuno bead reaction test/mixed antiglobulin <50% coated with antibody
- **Oligospermia:**
 - Sperm counts <15 million/ mL (*mild*), 5-10 million/ mL (*moderate*), below 5 million/ mL (*severe*).
- **Aspermia:** Means no semen
- **Azoospermia:** Means no sperm in semen
- **Asthenospermia:** No motile sperm or decreased motility

- A normal biopsy in an azoospermic man with a normal FSH level suggests obstruction of the vas deferens.
- Sertoli cell-only syndrome --- Absent germ cells on biopsy

LIVER FUNCTION TEST (LFT)

SGOT : SGPT Ratio (AST : ALT)

- Normally 1:1, In alcoholic liver diseases it is >2:1
- SGOT out of proportion to SGPT (very high SGOT) is seen in
 - Alcoholic hepatitis
 - Fatty liver of pregnancy (ratio is > 2:1)
- Aspartate aminotransferase, formerly called SGOT, is not as specific for liver disease as is ALT, which is increased in myocardial infarction, pancreatitis, muscle wasting diseases,

and many other conditions. However, differentiation of acute and chronic forms of hepatocellular injury are aided by examining the ratio of ALT to AST, called the **DeRitis ratio**. In acute hepatitis, Reye's syndrome, and infectious mononucleosis the ALT predominates. However, in alcoholic liver disease, chronic hepatitis, and cirrhosis the AST predominates.

- ALP is elevated out of proportion to serum transaminases (ALP >ALT) in diffuse **intrahepatic obstructive disease** which may be caused by some drugs or biliary cirrhosis, focal obstruction that may be caused by malignancy, granuloma, or stones in the intrahepatic bile ducts, or extrahepatic obstruction such as GB or CBD stones, or pancreatic or bile duct cancer
- GGT is greatly ↑ in obstructive jaundice, alcoholic liver d/s, and hepatic cancer. When the ↑ in GGT is two or more times greater than the ↑ in ALP, the source of the ALP is considered to be from the liver. When the increase in GGT is five or more times the ↑ in ALP, this points to a diagnosis of alcoholic hepatitis. GGT, but not AST and ALT, is elevated in the first stages of liver inflammation d/ to alcohol consumption, and GGT is useful as a marker for excessive drinking. GGT has been shown to rise after acute persistent alcohol ingestion and then fall when alcohol is avoided.
- Presence of urobilinogen in urine rules out any obstructive cause of jaundice
- Gall stones can be explained by precipitation of bilirubinate crystals in urine
- ALP is produced from bone, liver, intestine, placenta. Hepatic isoenzyme of ALP is heat stable
- Confirmation of elevation of ALP of hepatic origin is done by -5' nucleotidase. 5' nucleotidase & glutathione transferase are more specific for liver diseases
- Prothrombin time is a good indices of hepatic synthetic function
- GGT is a sensitive indicator of biliary tract disease
- SGOT is a mitochondrial enzyme released from heart, liver, kidney, skeletal muscles
- SGPT is a cytosolic enzyme released from liver.

- Direct bilirubin means conjugated fraction of total bilirubin. If direct bilirubin is >15% of total bilirubin, then it is called conjugated or direct hyperbilirubinemia.
- Initial investigation of choice in a case of obstructive jaundice is ---USG abdomen
- Low hemoglobin & elevated unconjugated bilirubin are typically seen with hemolytic picture

	Hemolytic	Hepato-cellular	Obstructive
c Hyper-bilirubinemia	Mainly unconjugated	Conjugated	Conjugated
c Vanden Bergh's reaction	Indirect	Direct/ Indirect	Direct
c Hb	Low	N	N
c Liver enzymes	N	Transaminases are elevated out of proportion to ALP	ALP is elevated out of proportion to transaminases
- SGOT, SGPT	N	↑↑↑	↑, N
- ALP	N	N, ↑	↑↑↑
c Urine :			
- Colour	Turmeric	Dark yellow	Dark yellow
- Urobilinogen (bile pigments)	+++ (turns dark on standing)	++	- (acholuric)
- Bilirubin	-	+	++
		(Bilirubinuria)	
c Stool			
- Colour	N	N in early phase	Clay colored/ pale
- Stercobilinogen	+	+	-
c Causes	hemolytic anemia	- Viral hepatitis - Toxic/ drug induced hepatitis - Toxic/ drug induce	Cholestasis Ca pancreas

IMP POINTS

- o The 3rd generation TSH detection methods can detect TSH levels as low as 0.004 mU/L.

- o A 25 year old infertile male underwent semen analysis. Results show: sperm count 15 million/ml; pH - 7.5; volume 2 ml; no agglutination is seen. Morphology shows 60 % normal & motile sperms. Most likely diagnosis is:

[AIPGMEE - 2002]

- A. Normospermia B. Oligospermia
C. Azoospermia D. Aspermia
(Ans: Oligospermia)

- o Arterial blood gas of a 5 year old child done at sea level gives the following results: pH 7.41, PaO₂ 100 mmHg, land PaCO₂ 40 mm Hg. The child is being ventilated with 80% oxygen. What is the (A-a) PO₂?

[AIIMS Nov'05]

- A. 570.4 mm Hg. B. 520.4 mm Hg.
C. 470.4 mm Hg. D. 420.4 mm Hg.
(Ans: 470.4 mm Hg)

$$\begin{aligned} \text{PAO}_2 &= \text{FiO}_2 (\text{P}_B - \text{P water}) + \text{PCO}_2 / \text{R} \\ &= 0.8 \times (760 - 47) + 400 / 0.8 \\ &= 0.8 \times 713 + 50 = 570.4 \end{aligned}$$

$$\begin{aligned} (\text{A-a})\text{PO}_2 &= \text{PAO}_2 - \text{PaO}_2 \\ 570.4 - 100 &= 470.4 \text{ mmHg} \end{aligned}$$

- o The blood gas parameters: pH 7.58, pCO₂ 23 mm Hg, pO₂ 300 mm Hg and oxygen saturation 60% are most consistent with:

[AIPGMEE 2003]

- A. Carbon monoxide poisoning
B. Ventilatory malfunction
C. Voluntary hyperventilation
D. Methyl alcohol poisoning
(Ans: Ventilatory malfunction)

- o A patient presents with HBs antigen positive, HBe antigen negative, anti-HBc IgG with HBV DNA 1000 copies, LFT is normal, USG shows no cirrhosis. Diagnosis is ---

[AIPGMEE 2010]

- A. Cirrhosis B. Chronic carrier state
C. Chronic hepatitis D. Acute hepatitis B
(Ans: Chronic hepatitis)

HBV-DNA is a marker of viral replication. Presence of HBs antigen and anti-HBc IgG both favours chronic hepatitis B

ANTI-OXIDANTS

Anti-oxidants / Free Radical Scavengers

- Free oxygen radicals & reactive oxygen species play a role in ageing & various d/s process
- Antioxidants act as protective scavengers.
- In radiation induced injury hydroxyl ion (OH^-) is generated from water. OH^- ion is the most reactive O_2 species, it causes injury by lipid peroxidation in cell membrane.

Free radical induced diseases

D/s by attacking cell membrane (Lipid peroxidation)	<ul style="list-style-type: none"> - ARDS - Retinopathy of prematurity - Bronchopulmonary dysplasia - Aging, Alzheimer's ds. - RA
D/s by attacking DNA (OH^- ion induced DNA hits) Redox regulated transcription factors	<ul style="list-style-type: none"> - AIDS - Cancers - Atherosclerosis - DM complications
Diseases by attack of proteins	<ul style="list-style-type: none"> - Channelopathies

Classification

Preventive A~	<ul style="list-style-type: none"> Natural: <ul style="list-style-type: none"> - Catalase - Glutathione peroxidase (Containing selenium) Synthetic <ul style="list-style-type: none"> - Chelators of metals - EDTA, DTPA - Desferrioxamine
Chain breaking	<ul style="list-style-type: none"> Phenols / aromatic amines. <ul style="list-style-type: none"> - Superoxide dismutase - Vit. E - Vit. C - Probucol.
Others	<ul style="list-style-type: none"> β-carotene (Vitamin A) Haptoglobin, hemopexin, transferrin, ceruloplasmin Urates Coenz Q

Drugs with anti-oxidant property

- Carvedilol
- Gliclazide
- Lamotrigine
- Selegiline (Deprenyl) & Rasagiline
- Probucol

NO (NITRIC OXIDE, EDRF)

Overview

- NO is synthesized from a/a arginine in presence of enzyme NO synthase (NOS). 5 redox cofactors are required NADPH, FAD, FMN, Heme & TH_4 bipterin.
 $\text{L-arginine} + \text{O}_2 \longrightarrow \text{Citrulline} + \text{NO} \longrightarrow \text{soluble guanyl cyclase} \longrightarrow \text{SM relaxation}$
- NOS 1 is found in brain, NOS 2 in macrophages and NOS 3 in endothelial cells.
- NOS 1 & 3 are activated by Ca^{++} (and also by agents \uparrow ing Ca^{++} eg. Ach, bradykinin & shear stress)
- Functions
 - SM relaxation in GIT
 - Vasodilatation,
 - Activation of macrophages/PMN ---Microbicidal
 - Inhibits adhesion & aggression of platelets

D/s a/w NO deficiency ---

- Hypertension, atherosclerosis
- Chronic intestinal pseudo-obstruction, Hirschsprung's d/s, achalasia
Inhaled NO is useful in t/t of --- PPHN in newborn, ARDS.
- D/s a/w NO --- GVHD, transplant rejection, bacterial sepsis (because of stimulation of NOS)

Drugs acting through NO (EDRF) ---

- Sildenafil
- Na-nitroprusside
- ANP
- Nitroglycerine
- Theophylline

[Mnemonic : SANTs]

GENERAL PHARMA

Routes of Drug Administration

- *Inhalational spray* Inhalational drugs :
 - Tobramycin
 - Azelastine
 - Posterior pituitary powder
 - Desmopressin
 - Steroids :- Flunisolide, fluticaproprionate, Triamcinolone acetonide, Beclomethasone & Budesonide
 - Insulin (under trial)
- *Transdermal* :

Fentanyl, Nitroglycerine, Hyoscine, Estradiol, Clonidine, Nicotine
- *Sub-lingual*:

GTN, Isoprenaline, methyltestosterone, clonidine, buprenorphine, DOCA

Drugs administered under supervision

Whole DOTS regime, in MDT Clofazimine and Rmp

Phases of clinical trials

	Trial	Study is conducted on	Establish	Remark
I	Non-therapeutic	Healthy human volunteers	Safety	Human pharmacological studies
II	Therapeutic exploratory	Patients	Efficacy	-
III	Therapeutic confirmatory	-	-	RCT are done, compared with standard drugs
IV	Post-marketing surveillance studies	-	-	

- Phase 0 trial is a new concept in which microdosing studies are carried out.
- To study the efficacy of a new drug B in comparison to the existing drug A, in treating a d/s type of drug trial which is best suited -- Phase 3 trials.
- Structural drug designing is preferred now a days becoz it relies on 3-D structure of biological target obtained through X-ray crystallography or NMR spectroscopy or computational models.

Examples of Pharmacogenetics

- Acetylator polymorphism
 - G6PD deficiency, Resistance to coumarin
 - Atypical pseudocholinesterase & Sch
 - Inability to hydroxylase phenytoin
 - Malignant hyperthermia by halothane
- Adenosine de-aminase deficiency is not included in pharmacogenetics
- Pharmacovigilance is related to drug safety

PRODRUGS

Prodrug	Active form
◦ Levodopa	- Dopamine
◦ α-Methyl dopa	- α-methyl nor-epinephrine
◦ Dipivefrin	- Epinephrine
◦ Enalapril	- Enalaprilat
◦ Proguanil	- Proguanil triazin
◦ Prednisone	- Prednisolone
◦ Bacamp/Talampicillin	- Ampicillin
◦ Sulfasalazine	- 5-ASA
◦ Cyclophosphamide	- Aldophosphamide, phosphoramidate-mustard, acrolein
◦ Sulindac	- Sulfide metabolite
◦ Fluorouracil	- Fluorouridine monophosphate
◦ Mercaptopurine	- Methylmercaptopurine ribonucleotide
◦ Primidone, phenobarbitone	- Phenobarbitol
◦ Fosphenytoin	- Phenytoin

→ Among ACE inhibitors Enalapril, benazepril, Quinapril, fosinopril, ramipril moexipril are prodrugs (But lisinopril and captopril are not)

DRUG METABOLISM

Drug interference by food

- Proton pump inhibitors (Omeprazole) should be taken at least 30 min before meal.
- Unionized drugs are well absorbed orally while highly ionized drugs (e.g. streptomycin & neostigmine) are absorbed poorly when given orally.
- Acidic drugs are unionized in stomach (salicylates/salicylic acid and barbituric acids) and absorbed in stomach.

- Presence of food interferes with absorption by forming insoluble complexes (Tetracycline + antacids/ Ca^{++}).

DRUG METABOLISM

Phase-I (non-synthetic) reactions:

Phase-II (Synthetic): To attach a conjugate to the drug molecule

Nonsynthetic or Phase I reaction

Attack functional group of drug molecule. Use cytochrome P450 monooxygenases

1. Oxidation (mostly)
 - N- or O- dealkylations
 - Oxidative deamination
2. Reduction
3. Hydrolysis
4. Decyclization

B. Synthetic or phase II reactions

To attach a conjugate to the drug molecule

1. Glucoronidation, conjugation
2. Acetylation
3. Methylation
4. Sulfation

→ Oxidation involves maximum drug metabolizing reactions, 50% of these use cytochrome P 3A 4/5

Drugs metabolising Cytochromes

- CYP3A4 : inhibited by Erythro, clarithro, keto-/itraconazole, verapamil, diltiazem, ritonavir, CCBs. Involved in biotransformation of largest number of drugs.
- CYP2C19 : Clopidogrel, PPI's.
- CYP2D6 : Carvedilol.
- CYP2D6 & 3A4 : Anti-retroviral drugs (ARTs).
- CYP B5 : Membrane bound hemoprotein which function as an electron carrier for oxygenases

- Phenobarb induces cytochrome 3A and 2B1
- Valproate and carbamazepine induce each others metabolism
- Phenobarb and phenytoin induce each others degradation by enzyme induction.
- OCP failure is seen with - Tetracycline, Rmp, Ampicillin, Phenytoin, Phenobarb (TRAPP)
- Theophylline dose should be reduced with - ciprofloxacin, Allopurinol, Cimetidine, Erythromycin, Contraceptives
- All ACE inhibitors are prodrugs except captopril & lisinopril

ENZYME INDUCERS

Drug	Enz/drug induced
Phenobarbitone	CYP3A, 2B1, phenytoin
Carbamazepine	Valproate
INH	
Rifampicin	CYP3A
Glucocorticoids	CYP3A
DDT, Chloral hydrate	

ENZYME INHIBITORS

Drug	Enz/drug inhibited
Allopurinol	Xanthine oxidase
Erythromycin,	
Ciprofloxacin	
Cimetidine	
Rifampicin	
Disulfiram	Acetaldehyde dehydrogenase, CYP2E1
INH	
Valproate	Phenobarbitone
Itraconazole, KTZ	

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Drugs which are not metabolized in liver

- Penicillin G (given parenterally it bypasses GIT & first pass metabolism)
- Synthetic estrogens (ethinyl derivative of estradiol)
Natural estrogens when given orally are inactivated in liver before reaching general circulation)
- Digoxin (safely given in liver diseases)

Drugs excreted unchanged in urine

- Digitalis
- Bretylium
- Methotrexate
- Sodium stibogluconate
- Acyclovir
- Gallamine
- Phenformin / metformin / chlorpropamide
- Gonadotropin
- Thiacetazone
- Aminoglycoside
- Neomycin
- Norfloxacin

[Usually ionized drugs are excreted unchanged in urine.]

Drugs with extensive first pass metabolism

These drugs preferably should not be given orally.

- Hydrocortisone
 - Morphine
 - Testosterone
 - Isoprenaline
 - Lignocaine
- [Mnemonic: HMT India Ltd.]

Quaternary ammonium (NH_4^+) compounds

- They do not cross BBB and have no CNS effects
 - Oral absorption is incomplete so used parenterally.
 - Examples
 1. Anticholinergics : Glycopyrrolate, Ipratropium, Oxyphenonium, Propantheline
 2. Neostigmine
 3. N-m blockers d-TC, Sch, Decamethonium
 4. Bromides
 5. Non-sedative anti-histaminics : Terfenadine, astemizole, Loratadine / cetirizine
 6. Heparin
- [Mnemonic: Plz GO IN HAL]

Drugs concentrated in

RBC	Fat	Collagen
Ethambutol Chloroquine	Clofazimine	Mepacrine

Therapeutic Drug Monitoring (TDM)

Serum level of drug has to be monitored when the patient is on therapy with ---

1. Drugs with low safety margin:

These are drugs with narrow therapeutic range or narrow index and exhibit *therapeutic window phenomena*. Examples are: Digoxin, anticonvulsants (phenytoin), antiarrhythmics (lignocaine), theophylline, cyclosporin, clonidine, TCA (imipramine), aminoglycosides, and glipizide.

2. Drugs with large individual variation : antidepressants, lithium

3. Potentially toxic drugs used in the presence of renal failure: vanco, aminoglycosides.
4. Poisoning cases

Monitoring while receiving drug therapy

- ATT --- Liver enzymes should be monitored
- Li --- Serum levels should be monitored
- Linezolid --- Platelet counts should be monitored (Netropenia, thrombocytopenia)
- Amphotericin B --- K^+ levels should be monitored as it can cause hypokalemia.

→ Serum levels are not monitored in warfarin therapy. Instead it is monitored by INR.

Therapeutic Index (TI)

High	Low	Very low
Penicillin, Cephalosporin, Macrolides	Chloramphenicol, Aminoglycoside, Tetracyclines [CAT]	Vanco, AmB, Polymixin [VAP]

Orphan drugs

Rare drugs for rare diseases. Baclofen, acetyl cysteine, Levothyroxine (T_3), digoxin fab Ab, desmopressin, sodium nitrite.

Drug Kinetic

	Zero order (linear)	First order kinetic
1. Rate of elimination	Const. (Saturation kinetic)	Proportional to drug concentration
2. $t_{1/2}$	↑ with dose	Constant
3. V and CL	CL progressively ↓es with ↑ing dose	Does not change with dose
4. Examples	Ethanol, salicylates (aspirin), phenytoin, tolbutamide, propranolol, warfarin, theophylline	Salicylates, phenytoin, tolbutamide etc.

→ Drugs whose kinetics changes from 1st order to zero order over the therapeutic range (Pseudo zero order) are phenytoin, tolbutamide, theophylline, warfarin, salicylate (aspirin), propranolol.

[Mnemonic: Warfarin ↑ses PTT]

Plasma Protein Binding (PPB) of a Drug

- Acidic drugs bind : Albumin
- Basic/alkaline drugs bind : α_1 acid glycoprotein.
- Drugs with high PPBs : Phenytoin, phenobarb, phenylbutazone, warfarin

Apparent volume of distribution (Vd)

- Vd of a drug describes the amt of drug present in the body as a multiple of that contained in unit volume of plasma

$$V_d = \frac{\text{Dose administered IV (D)}}{\text{Plasma concentration (C)}}$$

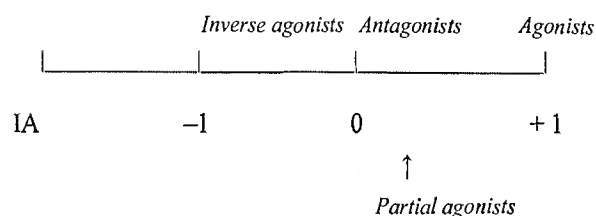
- V_d has low value for --- Drugs with high PPB (e.g. phenylbutazone, warfarin)
- V_d has high values for --- Drugs sequestered in body tissues V_d value much more than TBW (e.g. Digoxin V=6L/kg, propranolol, morphine)

- D/to large volume of distribution, digoxin, propranolol and morphine are not easily removable by hemodialysis in case of poisoning.
- Lipid insoluble drugs do not enter cells, V approximates ECF volume.
- Drug dosage is reduced in elderly bec / of ↓ body water, ↓ body mass & ↓ renal function.
- Loading dose is given to saturate tissue stores, it is mainly dependent on V_d
- Maintenance dose is mainly dependent on clearance (CL) i.e. plasma volume from which the drug is completely removed in unit time.

Agonist and Antagonist

- An antagonist has affinity but no intrinsic activity (IA=0)
- Partial agonists have affinity and submaximal IA (between 0 to 1) e.g. Nalorphine.
- Intrinsic activity and affinity both are important for drug action.

- Inverse agonists have affinity but intrinsic activity with a minus sign (IA between 0 to -1) e.g. DMCM.
- Agonists have both affinity and maximum intrinsic activity (IA = 1)



- A drug with preferential affinity for R_i (inactive receptor) will actually produce an effect opposite to that of an agonist and is k/as **inverse agonist**
- Efficacy**: Maximal response that can be elicited by drug.
- Potency**: Amount of drug needed to produce a certain response. Position of DRC on the dose axis is index of potency.

ANTIBIOTIC RESISTANCE

- First antibiotic resistance was observed among penicillins. penicillin group antibiotics acquired plasmid mediated resistance by producing penicillinase/ β -lactamase.
- To overcome the problem of β -lactamases broad spectrum cephalosporins were developed, which contained oxymino side chain. Cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone.
- Now a days bacteria have become more smart. Some strains of *Klebsiella pneumoniae* started producing ESBL (extended spectrum β -lactamases) and they are capable of hydrolysing all above drugs + aztreonams/monobactams. Carbapenems (meropenem > imipenem) are effective against these ESBL producing organisms.
- Resistance in methicillins & cephalosporins was d/to altered binding proteins at chromosomes.
- Resistance in chloramphenicol was d/to enzyme acetyl transferase by plasmids.
- Resistance to erythromycin was d/to methylation of ribosomes by plasmids.
- Resistance to quinolones was d/to methylation in topoisomerase IV.

Mechanism of resistance (enzymes)	M/c seen in	Antibiotics which are resistant	Effective antibiotics
1. Penicillinase	Most bacteria	Older penicillins,	Penicillinase producing Pn (Cloxa, oxa, Naf - cillins)
2. β -lactamase		Penicillins, narrow spectrum cephalosporins	β -lactamase inhibitors (Clavulunate + sulbactam), Broad spectra cephalosporins
3. Extended spectrum β -lactamases (ESBL)	Gram -ve/ Enterobacteria esp. <i>Klebsiella pneumoniae</i>	All above + monobactams,	Carbapenem (Meropenem, imipenem) cephamycin
4. Methicillin resistant staph. aureus (MRSA)	<i>Staph. aureus</i>	Older penicillins, Methicillin	Vancōmycin (DOC) Teicoplanin Linezolid, Daptomycin, Minocycline, Quinupristin, Cotrimoxazole Cipro/levoflox, Rmp
5. Vancomycin resistant enterococci (VRE)	Enterococci	Vancomycin	

SAFETY OF DRUGS IN

Pregnancy

Safe in pregnancy (Drugs which do not cross placental barrier)

Drugs contraindicated in pregnancy (teratogenic)

- Heparin
- Insulin
- TSH, ACTH
- INH, Rmp, ethambutol
- Vasodilator :
Methyldopa, hydralazine
- CCB (nifedipine)
- Anti arrhythmic :
Quinidine, dyspyramide & procainamide are relatively safe
- Lidocaine c/b given
- Anti-helminthic
- Piperazine
- Niclosamide
- Desmopressin
(for DI in pregnancy)
- Chloroquine
(DOC for R_x of malaria)
- Proguanil
(DOC for P_x of malaria)
- Acyclovir
- Antibiotics
- Penicillins,
- Macrolides (erythro)
- Most cephalosporins,
- Amoxicillin, ampicillin
- Among immunosuppressive drugs
- Azathioprine & cyclosporin (cat C) relatively safe
- Warfarin
(c/b given in 2nd trimester)
- Prophylthiouracil
- LMW Heparin can cross placenta but safely±
- Iodine / iodides
- Lithium
- ACE inhibitors, β -blockers
- Atropine
- Diazepam, Chloral hydrate
- Corticosteroid
- Phenytoin, valproate
- Busulfan
- Cocaine, Heroin, ethanol
- Progestins
- Retinoids (isotretinoin)
- Tamoxifen
- Ciprofloxacin,
Chloramphenicol
- Tetracycline
- Aminoglycosides
(e.g. streptomycin)
- Allopurinol
- Live vaccines
- Metronidazole
(in 1st trimester)
- Theophylline
- Other immunosuppressive drugs
- Warfarin (I & III trimester)

- For T/t of seizures in pregnancy phenobarbital is considered drug of choice
- Among Anti-thyroid drugs propylthiouracil is **DOC** (Acc. to CMDT), however it may cause aplasia cutis.
Radioactive isotopes are absolutely contraindicated in pregnancy.
- For T/t of UTI in pregnancy nitrofurantoin, ampicillin and cephalexin are safe (fluoroquinolones are contraindicated).
- Antitubercular regimen in pregnancy Rmp+ INH (Ethambutol may be added for 1st two months). Streptomycin is absolutely contraindicated
- **DOC** for prophylaxis of malaria in endemic area is proguanil and for treatment is chloroquine.
- For anticoagulation in pregnancy :-
Heparin (for 1st 12 weeks) → Warfarin up to 36 week → Heparin 1 week before delivery and after 2 days → restart warfarin in puerperium
- Heparin does not cross placenta. It is anticoagulant of choice in pregnancy. While unfractionated heparin is safe in pregnancy, LMW Heparin can cross placental barrier.
- Lidocaine is safe first line IV drug for ventricular arrhythmias in pregnancy. Among oral drugs quinidine has been found to be safe. Adenosine > verapamil for t/t of SVT
- For T/t of eclampsia Mg sulph is the **DOC**.
- For t/t of HTN oral drugs of preference are methyl dopa > hydralazine > CCBs > atenolol > labetalol in that order
- For hypertensive crisis labetalol, hydralazine, nitroglycerine can be used
- **DOC** for chlamydial infection in pregnancy --- Azithromycin (erythromycin is alternative)
- **DOC** for listeriosis in pregnancy --- Ampicillin

- Lactation suppressants like, Bromocriptine, OCP, pyridoxine, thiazides, nicotine should be avoided in lactating mothers.
- Bromocriptine, phencyclidine, Li, cycloserine, cocaine Mtx etc drugs are contraindicated during breast feeding.

Drugs safe in

Hepatic diseases	Renal diseases	Porphyria
<ul style="list-style-type: none"> • Digoxin • Ethambutol • Streptomycin • Chloroquine (DESC) 	<ul style="list-style-type: none"> • Doxycycline • Polymyxin-B • Penicillin • Adriamycin • Ceftriaxone • Cefoperazone • CPZ • Pefloxacin • Chloramphenicol • Erythromycin • Omeprazole • Dicloxacillin • Nafcillin • Clindamycin • Metronidazole 	<ul style="list-style-type: none"> • Glucocorticoid • Clonazepam • Streptomycin • Penicillin • Aspirin, acetaminophen • Atropine • Insulin • Pefloxacin • Opiates • Narcotic analgesics

Antibiotics which c/b given in liver d/s

- Ampicillin
- Cloxacillin
- 3rd gen. cephalosporins
- Aminoglycosides (CACA)

Breast feeding*

Safe	Contraindicated when mother is receiving
<ul style="list-style-type: none"> • Antacids • Erythromycin, cephalosporin • Propyl thiouracil • Warfarin • Digoxin • Insulin 	<ul style="list-style-type: none"> • Anticancer/cytotoxic drugs like Mtx, cyclophosphamide • Among antibiotics Tetracycline • Antithyroid drugs & Radioiodine (¹³¹I) • Dicumarol derivatives (Phenindione) • Ergotamine, gold salts, Li • Cimetidine

ADVERSE EFFECTS OF SOME DRUGS

Pseudotumor cerebri	<ul style="list-style-type: none"> • Gluco / Mineralocorticoids • Hypervitaminosis A • OCPs • Tetracycline • Amiodarone • Nalidixic acid • Hypoparathyroidism
Alopecia	<ul style="list-style-type: none"> • Ethionamide • Cytotoxic drugs • Heparin • OCP withdrawal • Li • Valproate

Pancreatitis	<ul style="list-style-type: none"> c Didanosine c Thiazides c Steroids c Melphalan c L-asparaginase
Polyneuropathy	<ul style="list-style-type: none"> c Amiodarone c Cisplatin c INH c Dapsone c Vincristine c Anti-retroviral drug
Pigmentation of skin	<ul style="list-style-type: none"> c Clofazimine, methysergide (red) c Nicotinamide (brown) c OCP (chloasma) c ACTH (hypermelanosis) c Senna (melanosis) c Amiodarone (violaceous pigmentation in sunlight) c Zidovudine, (nails) c Mepaerine, digoxin (yellow) c Phenothiazine c Chloroquine
Flu-like syndrome	<ul style="list-style-type: none"> c Methyl dopa c Rmp c Interferon c Clofibrate c Hydralazine Heta starch [Mr. RICH]
Dysgeusia (Altered taste sense)	<ul style="list-style-type: none"> c Li c TCA c Metronidazole c Zopiclone (metallic taste) c Sodium stibogluconate c ACE inhibitors c L-dopa
Fibrous gingival hyperplasia	<ul style="list-style-type: none"> c Nifedipine c Phenytoin
Livido reticularis	<ul style="list-style-type: none"> c Amantadine c Bromocriptine
Pure red cell aplasia	<ul style="list-style-type: none"> c Chlorpropamide c Azathioprine c Phenytoin, INH
Drugs Precipitating Gout (Hyperuricemic)	<ul style="list-style-type: none"> c Pzm, cthambutol c Thiazide c Frusemide c Ethacrynic acid c Diazoxide c Clofibrate c Cytotoxic drugs (Mtx) c L-dopa

Hypokalemia	<ul style="list-style-type: none"> c Ampho-B c Insulin
Lupus like syndrome /SLE	<ul style="list-style-type: none"> c INH c Methyl dopa c Phenytoin c Carbamazepine c Hydralazine c Procainamide c Penicillamine (IMP PHCs)
SIADH	<ul style="list-style-type: none"> c Chlorpropamide c Cyclophosphamide c Carbamazepine c Vincristine / vinblastine, Vasopressin c Vaso/desmo-pressin c Oxytocin c General Anesthetics c TCA c Nareoties c Indomethacin c Fluoxetine/ SSRI, c MAO inhibitors c Sulfonamides (CVO, ATN, IN, F, MTV, Sony channels)
DI/Polyuria	<ul style="list-style-type: none"> c Li c Demeclocycline c Thioridazine c Fosearnet c Methoxyflurane

Drugs affecting prolactin level

Drugs causing hypoprolactinemia	<ul style="list-style-type: none"> c Dopamine c Bromocriptine c Apomorphine c Ergometrine c Glucocorticoids 	<i>DA agonist</i>
Drugs causing hyperprolactinemia	<ul style="list-style-type: none"> c Chlorpromazine c Haloperidol c Metoclopramide c Reserpine c Methyl dopa 	<i>DA Antagonist</i> <i>DA depleter</i>

- Dopamine ↓ prolactin levels . so DA agonists cause hypoprolactinemia and v/v:
- Estrogen and thyroid hormones ↑ prolactin levels.
- Hyperprolactinemia (↑ prolactin levels) has negative feedback on estrogen so ↑ prolactin level causes ↓ estrogen.
- M/c dose limiting ad/e of colchicine is - GI (Diarrhoea)

Drugs causing important Syndromes

- Gray baby syndrome --- Chloramphenicol (In preterm babies)
- Fanconi syndrome --- Tetracyclines (Outdated tetracycline can cause PCT damage)
- Reye syndrome --- Salicylates (aspirin)
- Red man syndrome --- Vancomycin
- Hemolytic uremic syndrome (HUS) --- Mitomycin-C (m/c drug), cisplatin, bleomycin
- Tumour lysis syndrome --- Fludarabine t/t in pt of CLL
- Hand foot syndrome --- Capecitabine
- Mobius syndrome --- Misoprostol
- Sicca syndrome --- Sulfonamides

→ Rash of infectious mononucleosis is increased by ampicillin.

→ Allopurinol, cephalosporins, sulfonamides, barbiturates are a/w TEN & SJS which in later phase can cause Sjogren like syndrome.

→ Ceftriaxone can cause syndrome of pseudocholecystitis

Drugs causing Nephrotic Syndrome

- Gold
- Penicillamine
- Captopril
- NSAIDS
- Probenecid
- Trimethadione
- Mercury

Drug-induced pulmonary d/s

Pulmonary edema	Methadone Ritodrine (β_2 agonist) Propoxyphene
PPHN	Fenfluramine
Pulmonary fibrosis	Bleomycin Busulfan Methysergide Amiodarone
Pleural fibrosis	Practolol Busulfan
Retroperitoneal fibrosis	Methysergide
Bronchospasm	Aspirin, β -blockers
Hypersensitivity pneumonitis	Nitrofurantoin

→ Bleomycin causes destruction/ necrosis of type 1 pneumocytes, while hyperplasia and metaplasia of type 2 pneumocytes.

Drug-induced Liver d/s

Liver necrosis	Tetracycline, CCl ₄
Hypersensitivity hepatitis	Halothane
Macrovesicular steatosis	Glucocorticoids, estrogens, tamoxifen, amiodarone
Cholestasis	Anabolic steroids, chlorpropamide, chlorpromazine, cyclosporine, OCPs, clopidogrel

Drug-induced CVS d/s

Sinus Tachycardia	Theophylline Amphetamines Nifedipine Anti-cholinergics [ThANA]
Torsades' De Pointes (polymorphic ventricular tachycardia)	Quinidine, terfenadine, astimazole, procainamide, sotalol, thiazides, erythro, levoflox, CPZ
QT prolongation	Cisapride

→ Cisapride should not be co-administered with microsomal enzyme inhibitors like ketoconazole and erythromycin. May precipitate Torsades de pointes.

→ Dipyridamole worsens angina and causes coronary steal phenomena.

Pseudomembranous enterocolitis

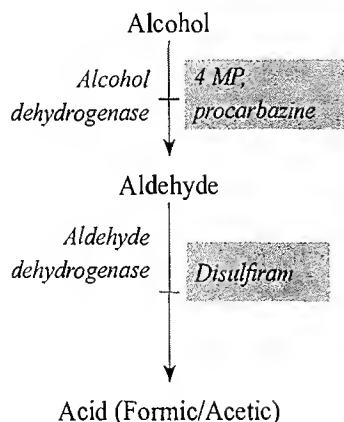
- Clindamycin
 - Tetracycline
 - Ampicillin
 - Cephalosporin
- [doc for T/t of P~ : Metronidazole > vancomycin]

Post antibiotic effect is seen with

- Fluoroquinolones,
- Aminoglycoside,
- Beta-lactamase inhibitor

DISULFIRAM

- Disulfiram inhibits aldehyde dehydrogenase



Drugs causing disulfiram reaction (Alcohol intolerance/ Deterrents)

- Procarbazine
- Cephalosporins (Cefoperazone, cefamandole, cefotetan)
- Metronidazole
- Moxalactam
- Sulfonamides ±
- Chlorpropamide
- Griseofulvin
- Nitrafazole
- Furazolidone
- Citrated calcium carbimide

Drugs in G-6-PD deficient

Drugs causing frequent hemolysis	<ul style="list-style-type: none"> Antimalarials Primaquine, quinine, pama / pentaquine Most sulfonamides (Sulfones, Dapsone) Analgesic & antipyretic (Aminopyrine, ASA) Probenecid, Antibiotics e.g. Streptomycin, INH, Nitrofurantoin, Furazolidone Oral hypoglycemics (Tolbutamide, chlorpropamide) Fava beans, Moth balls (naphthalene)
Drugs which cause hemolysis less frequently (Can be used with caution)	<ul style="list-style-type: none"> Chloroquine, mepacrine Sulfadiazine, Sulfafurazole Aspirin, phenacetin Chloramphenicol Ascorbic acid BAL
Drugs which DO NOT cause hemolysis	<ul style="list-style-type: none"> Estrogen Rmp Penicillin Prednisolone Pyrimethamine

Gynaecomastia

- Spironolactone
- Cimetidine
- KTZ

Oligospermia

- Chemotherapeutic drugs esp. cyclophosphamide, MOPP therapy in Hodgkin's lymphoma.
- Reversible oligozoospermia is seen with the use of methotrexate.
- Ketoconazole, cimetidine, spironolactone

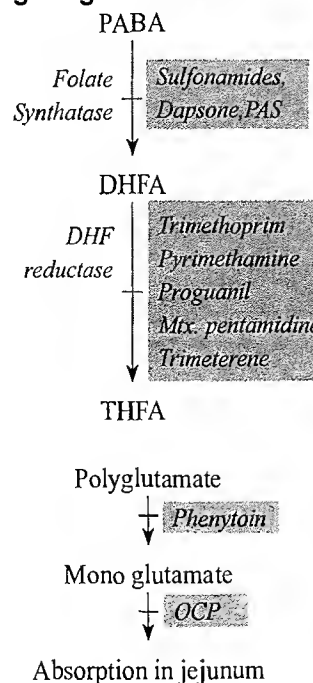
Drug producing pain & necrosis on injection

- IM - Cardiac glycoside, quinidine, Iron sorbitol, Progesterone, Streptomycin, Tetracycline
- IV - Sodium pentothal, propofol, tranexamic acid

1st dose effect is seen with

- Bromocriptine (marked ↓ in BP)
- Prazosin (postural hypotension)
- Gold (postural hypotension)

Drugs causing megaloblastic anemia



- Drugs which impair DNA metabolism also causes megaloblastic anemia
 - Purine antagonist: 6MP, azathioprine
 - Pyrimidine : 5- FU, cytosine arabinoside
 - Others : Procarbazine, Hydroxyurea, Zidovudine, Acyclovir, and Primidone

Drugs producing

Drugs causing	Drugs
Priapism	Trazodone
Rhabdomyolysis	Levostatin, gemfibrozil
Urinary retention	Anti cholinergics, TCA, Li, Some anti-hypertensive
Urinary incontinence	Phenothiazine
Peptic ulcer	Salicylates & corticosteroids
Parkinsonism	Phenothiazine
Osteoporosis	Heparin, phenytoin, Li
DLE	Hydralazine

MECHANISM OF ACTION OF DRUGS**Drugs acting on microtubules**

- Vinca alkaloids
- Colchicine (mitotic inhibitor)
- Paclitaxel
- Griseofulvin
- Mebendazole / Thiabendazole

Phosphodiesterase inhibitors

- Cilastatin (PDE-I)
- Amrinone, Milrinone (PDE-III)
- Theophyllines, Pentoxifylline ---are non selective PDE inhibitor
- Plicamilast: Selective PDE III/IV inhibitor which is responsible for bronchodilatation & anti-inflammatory action. Cilomilast and Roflumilast are under trial
- Sildenafil / 'viagra' (PDE-V): Causes release of NO locally resulting in vasodilation
- Dipyridamole (PDE-V)
- ADH, Prazosin, Krtotifen are partial inhibitors of PDE

Drugs inhibiting nucleic acid enzymes

Enzymes	Inhibited by
◦ DNA polymerase (DNA dependent DNA polymerase)	-- Cytarabine, vidarabine, acyclovir

- DNA dependent RNA polymerase -- Rifampicin
- Reverse transcriptase (RNA dependent DNA polymerase) -- Zidovudine
- Thymidylate synthetase -- 5-FU
- DNA Gyrase -- Quinolones (Ciprofloxacin), novobiocin, nalidixic acid
- DNA Topoisomerase -I -- Camptothecin, Irinotecan
- DNA Topoisomerase -II -- Anthracyclines (Doxo-, Daunorubicin, Etoposide, Teniposide)

→ Cytarabine inhibits intercalation of DNA

→ 5-FU is incorporated in both DNA & RNA

M/A of Antimicrobials

Drugs inhibiting	Example
Cell wall synthesis	Cephalosporins, cycloserine, vancomycin, bacitracin, streptogramins
Protein synthesis	Chloramphenicol, erythromycin, clindamycin
DNA gyrase	Fluoroquinolones

Drugs causing leakage from cell membrane

- Polymyxin
- Colistin
- Amphotericin B
- Nystatin (K⁺ leakage from cell membrane)
- Bacitracin The target for all these drugs is the polysomes (polyribosomes) in the bacterial cytoplasm

Drugs acting on protein synthesis

- The target for all these drugs is the polysomes (polyribosomes) in the bacterial cytoplasm.
- Inhibition of protein synthesis catalyzed by 70 S ribosomes

70 S	70/80 S ribosomes
Aminoglycosides	Tetracycline
Spectinomycin	
Chloramphenicol	
Clindamycin	
Erythromycin	
Linezolid	
(fusidic acid)	

Aminoglycoside (Streptomycin) — Binds to the 30 S subunit of ribosome & distorts its structure, interfering with the initiation of protein synthesis

Tetracycline — Blocks access of the aminoacyl t-RNA to the mRNA ribosome complex by interacting with small ribosomal subunits

Puromycin — Structural resemblance to aminoacyl t-RNA & gets incorporated into growing peptide chain causing inhibition of elongation

Chloramphenicol — Binds to 50S ribosome & inhibits prokaryotic peptidyl transferase

Macrolides Erythro/clindamycin — Binds irreversibly to 50S ribosome & inhibit translocation

Diphtheria toxin — Inactivates eukaryotic elongation factor eF-2, thus preventing translocation

Linezolid — Binds to 23 S fraction of 50 S ribosome & interferes with formation of N-formyl methionine – t RNA – 70S initiation complex

[Mnemonics : 1. Aminoglycoside initiates as 'a' is the first letter (or remember strepto starts), 2. T for t RNA 3. In macrolides lides for location]

PENICILLINS

	Penicillinase Resistance	Acid stability	Remark
• Benzyl penicillin (Pen G)	-	-	Narrow spectrum antibiotic
• Benzathine Pn G	-	-	Longest acting
• Procaine PenG	-	-	-
• Pen V (phenoxymethyl Pn)	-	+	Narrow spectrum Pn
• Methicillin	+	-	Anti-staphylococcal Pn
• Oxacillin	+	+	" "
• Nafcillin	+	+	Partially acid resistant
• Cloxa & Dicloxacillin	+	+	
• Amoxiclav (Augmentin)	+	+	Extended spectrum Pn, β - lactamase inhibitor
• Ampicillin	-	+	Food interferes with absorption, causes diarrhoea
• Amoxicillin	-	+	
• Carbenicillin, Ticar/ piper	-	-	Anti-pseudomonal Pn, not effective Vs anaerobic streptococci
• Carbenicillin	-	+	

→ Aminoglycosides bind to the 30S subunit and block initiation of protein synthesis by forming aberrant initiation complexes. In addition, they cause miscoding at the aminoacyl-tRNA-mRNA step.

→ Chloramphenicol and clindamycin inhibit peptidyl transferase.

→ Tetracycline inhibits binding of aminoacyl-tRNAs at the A site.

→ Erythromycin & spectinomycin inhibit translocation.

→ Fusidic acid forms a ternary complex in which the drug is bound to the ribosome together with elongation factor G in its ADP-bound state although movement of the tRNA-peptide occurs from the A to the P site.

→ Linezolid binds to 23S RNA of the 50S ribosomal subunit.

→ Benzathine Pn is longest acting Pn. Does not cross BBB.

→ Procaine Pn is DOC for neurosyphilis

→ Ureidopenicillins are---Azlocillin, mezlocillin, Piperacillin

→ Orally as well as parenterally effective Pn : Amoxicillin, Cloxacillin

→ Anti staphylococcal and penicillinase resistant Pn : (MONC)--- Methicillin, Oxacillin, Nafcillin, Cloxacillin

→ If a patient develops severe hypersensitivity to a penicillin, all other β lactam antibiotics are contraindicated except aztreonam.

• Cilastatin: Reversible inhibitor of dehydropeptidase. Combined with imipenem to prevent renal hydrolysis of it.

DOC for Staphylococcal Aureus

1. Non-penicillinase producing -- Pen G /Pen V oral)
2. Penicillinase resistant --- Penicillinase producing or beta lactamase inhibitors (cloxa-, oxa-, Naf- cillins)
3. MRSA --- Vancomycin ± Genta ± Rmp

Anti-pseudomonas drugs

- Azlocillin
- Ceftazidime
- Aztreonam
- Piperacillin
- Cefotaxime
- Cefepime
- Ciprofloxacin, Oflox
- Amikacin
- Gentamycin
- Moxalactam
- Mezlocillin
- Cefoperazone
- Imipenem
- Carbenicillin
- Ticarcillin
- Colistin
- Pefloxacin, levoflox
- Meropenem

Penicillins do not cause

- Disulfiram like reaction
- Pseudomembranous enterocolitis
- Optic neuritis

Penicillins do not precipitate

- Porphyria
- Hemolysis in G-6-P-D deficient Patient

CEPHALOSPORINS

- 1st generations are effective Vs. Gm⁺
2nd generations are effective Vs. Gm⁻
3rd generations are effective Vs. Gm⁻ including pseudomonas (esp. Ceftazidime, Cefoperazone)
- 4th generation cephalosporins are : **cefpirome, cefepime.**
- 5th generation cephalosporins are : - **ceftobiprole, ceftaroline.**
- Disulfiram like reaction (Alcohol intolerance) :
 - Cefoperazone
 - Cefamandole, Cefotetan
 - Moxalactam
- Cephalosporin which causes bleeding & coagulopathy more often than other cephalosporins : Moxalactam
Moxalactam > Cefoxitin > cefoperazone, cefotitan
- Safe in renal failure/disease (Dose reduction is not reqd.)
 - Cephalixin
 - Cefaclor
 - Cefoperazone
 - Ceftriaxone

- Most nephrotoxic --- Cephaloridine
- Cefixime and Cefpodoxime proxetil are orally active 3rd generation cephalosporin
- Effective against penicillinase resistant *gonococci* --- ceftriaxone.

FLUOROQUINOLONES

- Longest half life : Sparfloxacin (15-20 hr) > Moxi (12h)
- 2nd generation fluoroquinolones are : Lome-, levo-, spar-, gati- and moxi- floxacin.
- Pefloxacin has highest CSF penetration : preferred in meningitis.
- D/to long half life and persistence in tissue lomefloxacin c/b given as single daily dose.

AMINOGLYCOSIDE

- Bactericidal, they inhibit **initiation** of protein synthesis by inhibiting 30 S ribosomes.
- Post antibiotic effect is seen.
- Curare like effect [*Neomycin & streptomycin should not be used with d-TC*]
- Ionize in solution (*not given orally*).
- Distribution is extracellular (**do not cross BBB /CSF**)
- Excreted unchanged in urine.
- Ad/E

	Most	Least
1. N-m blockade	Neomycin, streptomycin	Tobra
2. Ototoxicity	Strepto	Netilmycin
3. Nephrotoxicity	Genta	Strepto

- Topically used → Framycetin & Neomycin
- *Amikacin* has resistance to bacterial aminoglycoside inactivating enzymes, broadest spectrum among all aminoglycosides.
- *Gentamycin* is obtained from *Micomonospora purpurea*. Its plasma t_{1/2} is 2-4 hours after i/m injections. Highly nephrotoxic. Therapeutic index is low.

ANTI-MALARIALS

• Tissue schizonticides

Act in the liver to eliminate developing exoerythrocytic schizonts or latent hypnozoites. (e.g. - Primaquine)

• Blood Schizonticides or suppressive agents

Kill *blood* schizonts (e.g. chloroquine, amodiaquine, proguanil, pyrimethamine, mefloquine, quinine, halofantrine, artemisinin etc but not primaquine). Artemisinin derivatives are fastest acting erythrocytic schizonticidal while pyrimethamine is slow acting blood schizonticide.

• Gametocides

Drugs that prevent infection of mosquitoes by destroying gametocytes in the blood. (*Primaquine* for P. Falciparum and *chloroquine* for Pv, Pm, Po)

• Sporonticidal

Drugs that render gametocytes non-infective in the mosquito (e.g. Pyrimethamine, Proguanil)

Quinine

- Is erythrocytic schizonticidal for all species of plasmodia.
- Ad/e: hypoglycemia, thrombocytopenia (antibody mediated), cinchonism
- *Quinine is safe antimalarial for use in pregnancy. It should be used for life threatening infection.*
- IV Quinine is DOC for cerebral malaria & severe falciparum malaria (Artemisnine compounds in combination therapy preferred now a days)

Primaquine

- It is a tissue schizonticidal but not effective against blood schizonts (not useful as suppressive agent)
- Effective in both primary and secondary tissue phases.
- It is highly active against gametocytes and hypnozoites of P. vivax.
- Primary indication of its use is radical cure of relapsing malaria.
- Primaquine is the m/c antimalarial drug producing hemolysis in G 6-P-D deficient individuals. Contraindicated in G6-P-D deficient individuals & in pregnancy.

→ For casual prophylaxis is aimed to attack pre erythrocytic phase (in liver)

- Proguanil. (falciparum)
- Primaquine (All sps)

→ Radical cure is required in relapsing malaria to attack exo-erythrocytic stage.

- Primaquine (for ovale and vivax) is added to chloroquine/ Amodiaquine

Extract

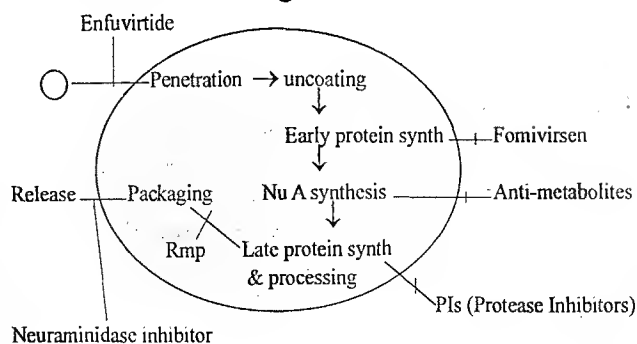
- For t/t of malaria in pregnancy— DOC is chloroquine. Quinine can be used for life threatening infections
- Proguanil is safe for prophylaxis against malaria in pregnancy, and along with chloroquine for prophylaxis in low endemic zones.
- Mefloquine is DOC for chemoprophylaxis against chloroquine resistant or multi drug resistant falciparum malaria
- First line t/t recommended by WHO now a days for t/t of uncomplicated falciparum malaria —Artemisinin based combinations (ACT : Artesunate (4 mg/kg qd x 3 d) + sulfadoxime (10 mg/kg)/pyrimethamine)
- Chloroquine retinopathy is predisposed by --- renal failure, duration of use >5 years, daily dose >3 mg/kg/d of chloroquine, cumulative dose >100 gram.

ANTI-PARASITIC DRUGS

- Amoebiasis --- Iodoquinol /paramomycin (for asymptomatic carrier state, eradication of cyst)
--- Metronidazole IV/oral (for invasive ds/ colitis, amoebic liver abscess)
- Cryptosporidiasis --- Nitazoxanide, which acts by inhibiting PFOR dependent e⁻ transfer in protozoa.
- Kalazar (Leishmaniasis) --- Antimony compounds (sodium stibogluconate)
--- Pentamidine & AMB are alternative
[D/to widespread resistance to antimonial compound in Bihar, Pentamidine & AMB are recommended]. Sitamaquine, Miltefosine, paramomycin allopurinol also useful
- Chagas'd/s(T. cruzi)--- Nifutrimox or beznidazole
- Trypanosomiasis --- Melarsopralol (for east african T~)
--- Pentamidine (for west african T~)
- Toxoplasmosis --- Pyrimethamine + sulfadiazine/ clinda
- Strongyloidiasis --- Ivermectin
- Schistosomiasis --- Praziquental
- Taeniasis solium --- Praziquental

ANTI-VIRAL DRUGS

M/A of Antiviral drugs



Preferred Antiviral drugs for

- For RSV --- Ribavirin (a synthetic nucleoside effective in bronchiolitis) & Palvizumab
- For CMV retinitis --- Ganciclovir (foscarnet is alternative)
- For influenza --- Zanamavir and oseltamivir
- For Swine flu --- Zanamavir (Relenza) and oseltamivir (Temiflu)
- For HPV --- Intralesional IFNs are useful against verruca vulgaris and condyloma acuminata. Imiquimod, an immunomodulator is also effective
- For HBV --- Interferons α_{2A} & α_{2B} , Adefovir, lamivudine in low dose for chronic Hepatitis B
Nucleoside RT/DNA p inhibitors enteca-/tenofo vir, telbivudine, clevudine, emtricitabine)
- For chronic HCV --- Pegylated interferons α_{2A} & α_{2B} are DOC
- Herpes viruses --- Cidofovir is active against all human herpesviruses (nucleotide analog)

→ Chronic Hepatitis B is treated with Lam/IFN α while chronic hepatitis C is treated with peg IFN α + Ribavirin

→ Fomivirsen is the first anti-sense oligonucleotide and is active against CMV retinitis.

→ Most imp ad/e of abacavir is fatal hypersensitivity syndrome

→ Docasanol, a long chain saturated alcohol, c/b used topically for herpes labialis. Acts as fusion/entry inhibitor

ANTI-RETROVIRAL DRUGS (ART)

Reverse transcriptase inhibitors (RTI)

Nucleoside RTI (NRTI)	Non Nucleoside RTI (NNRTI)
• Zidovudine	• Dela-vir-dine
• Zalcitabine	• Efa-vir-enz
• Abacavir	• Ne-vir-apine
• Lamivudine	• Eta-vir-ine
• Stavudine	
• Didanosine	
• Emtricitabine	

Nucleotide RTI	Entry Inhibitor
• Adefovir	• Enfuvirtide
• Tenofovir	• Maraviroc

Protease inhibitors (PIs)	Integrase Inhibitor
• Ampre-navir	• Raltegravir
• Indi-navir	
• Nelfi-navir	
• Rito-navir/lopi-navir	
• Saqui-navir	
• Fosqmpre-navir	

Imp. mnemonics to remember:

1. Nucleoside RTIs : ZiZa Ab Left SiDE :
2. Nucleotide RTIs : TA(I)D = Tenofo, Adefo
3. Non- Nucleoside RTIs : " vir" is the middle word in all NNRTI i.e. Delavirdine, Efavirenz, Nevirapine [except enfuvirtide]
4. PIs : " navir" is the last word in all PIs
5. Entry inhibitor is : Enfuvirtide

- Efavirenz acts by inhibiting HIV-1 reverse transcriptase. It is the drug which can be given to a patient of HIV who is already on ATT.

Enfuvirtide

- It is recently introduced HIV derived synthetic peptide which acts by binding to HIV-1 envelope glycoprotein (gp41) and preventing fusion of viral and cell membranes (fusion inhibitor/ entry inhibitor)
- It is not active against HIV-2.
- Given subcutaneously.

Newer ART

- Maraviroc is a CCR5 (chemokine receptor 5) inhibitor for HIV-1.
- Raltegravir is an integrase inhibitor against HIV.

Ad/e of ART

Ad/e	Caused by
Peripheral neuropathy	Stavudine (71%), didanosine (20%), zalcitabine <i>NOT</i> seen with zidovudine > lamivudine
Pancreatitis	Didanosine > Lami
Lipodystrophy	Stavudine, all PI's
Lactic acidosis	NRTI's
BM depression	Zidovudine
Myopathy	Zidovudine
Hypertriglyceridemia	Ritonavir
Steven Johnson syndrome	NNRTI, Abaca, Virs (Amprena, Daruna, Fosamprina, Tiprana)

- Lamivudine and Emtricitabine are best tolerated NRTIs
- Stavudine has max^m chances of causing lactic acidosis and it is most strongly a/w lipodystrophy among all NRTIs
- All PIs(-virs) are metabolized by liver and can cause lipodystrophy
- Skin rashes are seen with NNRTIs. Nevirapine can cause SJS and TEN
- NOT effective against HIV-2 : Nevirapine, efavirenz, enfuvirtide

- **Tesamorelin** is an analogue of GRF. It is the first and only t/t indicated to reduce excess abdominal fat in patients of HIV induced lipodystrophy.

Combination which should be avoided are

- Zidovudine + Stavudine : P h a r m a c o d y n a m i c antagonism
- Stavudine + Didanosine : Toxicity ↑es (lactic acidosis)
- Lamivudine + Didanosine : Clinically non-additive
- Lamivudine + Zalcitabine: In vitro antagonism

HAART

- Includes use of 3 or more drugs of which 1 or 2 are NRTIs.
- May be 2 NRTIs + 1 PI or INRTI + 1 NNRTI + 1 PI
- For post exposure prophylaxis: 2 NRTI (routine exposure) or 2 NRTI + 1 additional drug for high risk exposure

- Zidovudine toxicity is ↑ by --- Probenicid, cisplatin, cyclophosphamide
- All NRTIs are excreted by kidney and require dose adjustment in renal d/s except Abacavir
- Protease inhibitors are metabolized by cytochrome P450, so inducer e.g. rifabutin should be avoided
- Ritonavir is best used as a pharmacokinetic booster of other protease inhibitors
- Enfuvirtide is the first drug in the new class of fusion inhibitors, which blocks the entry of HIV into cells.
- Drug useful for PCP in AIDS patient --- oral cotrimoxazole (DOC) & intermittent inhaled pentamidine
- Drug safe in pregnancy with HIV --- zidovudine. Alternatively single dose 200 mg Nevirapine c/b used to prevent vertical transmission. Delavirdine and Efavirenz should also be avoided in pregnancy
- Thioacetazone should not be used in HIV positive patients because it causes serious toxicity. The major adverse effects are--hepatitis, dermatitis, SJS, and rarely BM depression.

ANTI-TUBERCULAR DRUGS

- **Safe in liver d/s**
Azithro/ Clarithro, Ethambutol, Rifabutin, Streptomycin
Patient with hepatic d/s should be treated with--- Ethm + Streptomycin (If required INH + Rmp cautiously)
- **Safe in renal d/s ---**
Rifabutin (absolutely safe) > Rmp
Azithro, Clarithro, Ethambutol, INH, Pzm, also
ATT Regimen in CRF :
INH + Rmp + Pzm (+ Etham for 1st 2 month)
- **Safe in pregnancy**
INH, Rmp, Ethm, Azithromycin, Rifabutin
[streptomycin is contraindicated]
ATT Regimen in pregnancy :
INH + Rmp x 9 month (+ Ethambutol for first 2 month)
- **Regimen in HIV infected patients ---4 drugs**
INH + Rifabutin + Pzm + E/S for 6 months
[Thioacetazone (Amithiozone) is avoided in HIV infected patients b/of serious G.I. & skin toxicity].
- Prolonged INH therapy can lead to pyridoxine deficiency → Peripheral neuritis is the most important dose dependent ad/e of INH therapy.
- Pyridoxine is given prophylactically with INH to prevent neurotoxicity (It prevents formation of hydrazone toxic complex)
- ATT which cross BBB: Pzm, ethionamide, cycloserine

Property	INH	Rmp	Pzm	Ethambutol	Streptomycin
Most effective Vs bacilli	Rapid/ fast growers population	Slow growing (persisters/ dormant bacilli)	Fast growing	multiplying	extracellular
Acts on cell	Extra + intra	Intra	Intra	--	extra
Acts on medium	acidic/ basic	--	acidic		alkaline
Crosses BBB	++ (penetrates all body cavities)	+	+	+	--
M/A	Inhibit mycolic acid synthesis	DNA dependent RNA polymerase		(incompletely)	Tuberculostatic
Other features	Max ^m drug resistance in India	Derived from Strepto. mediterrans		Patient's acceptability good	
Ad/ E	Sideroblastic anemia Pellagra like rashes Optic neuritis Peripheral neuropathy SLE / lupus Hepatitis	Resp-, cutaneous abd-, flu-like synd	Fulm. hepatitis Hyperuricemia	Optic neuritis Hyperuricemia	Ototoxic & vestibulotoxic
Contraindication			most hepatotoxic Liver d/s Pregnancy		Pregnancy

- Most effective regime for MAC: Ethm + clarithromycin
- Neuropsychiatric manifestation are seen with --- Cycloserine > INH
- All 1st line ATT are cidal except ethambutol.

ANTI HYPERTENSIVE OF CHOICE IN ---

Situation	Preferred
DM Type-1 + proteinuria (glomerulopathy)	ACE inhibitors
CRF + DM	ACE inhibitors
Heart failure, CHF or LV systolic dysfunc ⁿ	ACE inhibitors
Isolated systolic hypertension in elderly	Diuretics > CCB
Angina	CCB & β -blockers
Post MI patient	β -blockers, ACEi
Pregnancy	Methyldopa, hydralazine, CCB.

- Phentolamine is a $\alpha_1 + \alpha_2$ blocker and is DOC in hyperadrenergic states (hypertensive crisis) like pheochromocytoma, cheese reaction, clonidine withdrawal.

- Anti-hypertensive C/Ind in Pregnancy - ABD
ACE inhibitors, β -blockers (caution), Diuretics.
ACE inhibitors are absolutely contraindicated in pregnancy
- In a renal d/s patient with U/L renal artery stenosis --- ACE inhibitors are preferred antihypertensive.
[But remember that ACE inhibitors are contraindicated if there is B/L renal a. stenosis (here CCBs can be given)]
- Centrally acting anti-hypertensives --- Clonidine & methyldopa

- In hypertensive patients with Raynaud's phenomena and other peripheral vascular diseases and migraine CCBs are especially suitable. Beta blockers are esp. suitable for migraine prophylaxis.
- In hypertensive patients with gout, PVD, DM, Post MI, hyperlipidemia **ACE inhibitors are preferred.**
- Diuretics such as thiazides and frusemides are contraindicated in patients with hyperuricemia because they may precipitate gout.
- ACE inhibitors, ARB's & diuretics should be stopped 24 hours prior & diuretics 8-12 hr prior to surgery to prevent intraoperative hypotension.

ANTI FUNGAL DRUGS

- o M/A
 1. Drugs that disrupt fungal cell membrane
 - AMB, KTZ, Flu, terbinafine (Polyenes & azoles)
 2. Drugs that inhibit mitosis – Griesofulvin
 3. Drugs that inhibits DNA synthesis – Flucytosine
- o **Topically used anti-fungal drugs are** — Clotrimazole, Econazole, Flucanazole, Miconazole Nystatin etc.
- o **Anti-fungals which are used only orally** — Griseofulvin, KTZ (not by other route)
- o Tioconazole is topically effective for nail infections
- o Voriconazole & posaconazole are more effective against aspergillus. Caspofungin is effective in invasive candidiasis.
- o **Candins** act by inhibiting fungal wall synthesis. Active against candida and aspergillus.
- o **Voriconazole** is a broad spectrum triazole effective against invasive aspergillosis, resistant candidiasis, fusarium, febrile neutropenia unresponsive to antibacterial therapy.
- o **Itraconazole** is used IV or oral . In oropharyngeal candidiasis.
- o **AMB (Amphotericin -B)** : DOC for cryptococcal meningitis + HIV.

OPIOIDS

- o **Pure agonists**
Morphine, methadone, meperidine, propoxyphene, levorphanol, codeine
- o **Partial agonists (Weak agonists)**
Buprenorphine, butorphenol
- o **Pure antagonists**
Block all opioid receptors. E.g. Naloxone, Naltrexone, Nalmefene (not hepatotoxic) [3 'Nal']
- o **Endogenous peptides**: Endorphins have major action on μ while dynorphins act mainly on κ and enkephalins act on δ receptor. Nociceptin acts on orphanin (N/OFQ or ORL1) receptors.
- o In buprenorphine analgesia is good, ceiling effect⁺ & respiratory depression is there which is not reversed by naloxone.

Comparative properties of opioids & related drugs

	Analgesia Potency	Efficacy	Addiction liability	Resp depress ^a	Constipa ^a
Morphine	1	1	1	1	1
Methadone	1	1	1	1	1
Codeine	0.1	0	<1	<1	
Pethidine (Meperidine)	0.1	1	1	1	<1
Heroin	3	3		>1	
Fentanyl	100			100	
Pentazocine	-		<0.1	0.5	-
Buprenorphine*	25		<1		1

	Mu (μ)	Delta (δ)	Kappa (κ)	Remark
Morphine	+++	+	+	Agonist on all receptors μ , δ , κ but affinity for μ is higher
Methadone	+++			Long acting, preferred for opioid maintenance
Etorphine	+++	+++	+++	
Levorphanol			+++	
Nalorphine	---		+	
Nalbuphine	--		++	
Pentazocine		Partial agonist	++	
Sufentanil	+++	+	+	
Fentanyl	+++			
Buprenorphine	+		-	Partial agonist at μ & antagonist at κ receptors. Used for opioid maintenance/long lasting painful condit ^{ns}

- Naloxone is used for t/t of opioid overdose (e.g. in opioid induced constipation). DOC for morphine toxicity.
- Naltrexone c/b used for rehabilitation of alcoholics (in t/t of alcohol dependence)
- Methadone (or alternatively buprenorphine) c/b used for opioid maintenance.
- Nalmefene has longer half life than naloxone.

- o **Epidural opioids** act through mu (μ) receptors located in substantia gelatinosa present in DHC (dorsal horn cells) of spinal cord.
- o M/s rigidity progressing to severe stiffness d/to opioids is because of its effect on mu (μ) receptors.

- Butorphenol is the only opioid preparation available in nasal formulation.
- Etorphine** is an agonist on mu, kappa, and delta receptors with equal affinity for all the 3 receptors.
- Fentanyl and its congeners** are mu (μ) receptor agonists. Analgesic efficacy is different
Sufentanil > fentanil = remifentanyl > morphine
 Potency:
Sufentanil > fentanil > morphine

Sufentanil is the most potent opioid analgesic (10 times than fentanyl and 1000 times more potent than morphine, whereas pethidine (meperidine) and propoxyphene are the least potent. Alfentanil is seldom used now.

- Papavarine has least narcotic potential.
- Nor-pethidine has seizures inducing properties.
- Meptazinol, dezocine are agonist / antagonist opioid
- Meptazinol** is a partial opioid agonist. It \downarrow the Jarisch-Herxheimer reaction in Louse borne relapsing fever.

ANTI-HISTAMINICS

	Location	Agonist	Antagonist
H ₁	SM, CNS endothelial cells	Histamine, promethazine	Chlorpheniramine
H ₂	Gastric parietal cells, cardiac m/s,	Dimaprit	Ranitidine
H ₃	CNS origin cells	(R) histamine	Thioperamide Clobenpropit
H ₄	Hemopoietic	Clobenpropit	Thioperamide

- Quickest acting --- Terfenadine
- Longest acting --- Astemizole
- Least sedative --- Loratadine > Astemizole
- Azelastine is topically active anti-allergic drug. It blocks H₁ & LT receptor.
- Rupatadine** is recently introduced antihistaminic with additional PAF antagonist property.
- Ebastine** is a new second generation non-sedative anti-histaminic that is converted in carbostine.
- Non sedative anti-histaminic compounds are (N-ALCAT) Astemizole, loratidine, cetirizine, azelastine, terfenadine.
- Terfenadine** is a/w Torsades de pointes (ventricular

tachycardia) when given along with drugs that inhibit metabolism like erythromycin, KTZ.

DOC for various sicknesses

Motion sickness	--- Hyoscine (transdermal patch)
	--- Cyclizine, Meclizine also useful.
Sea sickness	--- Meclizine
Morning sickness	--- Dicyclomine (better), Promethazine
Mountain sickness	--- Acetazolamide

Histamine

- Synthesized from histidine
- Secreted by mast cells, basophils and other cells like gastric mucosal cells and brain cells.
- Functions :
 - Via H₂ receptors -
 \uparrow in gastric acid secretion through parietal cells.
 - Dilatation of small blood vessels, constriction of visceral SM (bronchospasm),
 - Also related to arousal, sexual behaviour, hypotension, and sensation of itching.

Serotonin Syndrome

- Life threatening condition d/to excess serotonergic activity in CNS and peripheral serotonin receptors.
- Caused by
 - SSRIs
 - TCA
 - Sumatriptans
 (NOT caused by RIMAS i.e. reversible inhibitors of MAO)

Anti-Tussives

- Anti-tussive which acts by decreasing the sensitivity of stretch receptors \rightarrow Benzonatate

ANTI-EPILEPTIC DRUGS

Phenytoin

- Exhibits **saturation (zero order) kinetics**. Kinetics changes from first to zero order within the therapeutic concentration.
- Enzyme inducer - Phenytoin is a potent inducer of hepatic

microsomal enzymes & induces metabolism of its own and of carbamazepine, warfarin, steroids, thyroxine, TCA, doxycycline

- Drugs that inhibit its metabolism (causing its plasma concentration to rise) are — valproate, cimetidine, cotrimoxazole, INH
- PPB is 90% (very high). It should not be given i/m.
- Fosphenytoin is the prodrug
- Uses — All types of partial seizures. Generalized seizures & status epilepticus also respond but it is not used for absence seizures.

Ad/E

CNS : Sedation, seizures, **cerebellar symptoms** at toxic doses (ataxia, nystagmus, diplopia, vertigo etc.)

Hemat — Megaloblastic anemia, vit K deficiency, vit D deficiency (Rickets and osteomalacia)

Skin — Hirsutism, rashes, coarsening of facial features

Others — Dupuytren's contracture, pseudolymphoma, osteomalacia, gingival hyperplasia, Hyperglycemia because phenytoin is an inhibitor of insulin secretion

Newer Anti-Epileptic Drugs (AED)

	M/A	Remark
Locasamide	Slow inactivation of Na ⁺ channels	Adjunctive t/t of partial Sz ± 2 ^o generalisation
Lamotrigene	Inhibits voltage gated Na ⁺ channels	Monotherapy in >12yr partial Sz/GTCS
Levetiracetam	Binds to synaptic vesicle glycoprotein 2A (SV2A) receptor	Effective in IGE (Idiopathic generalised epilepsy), Kindled Sz but ineffective in PTZ induced Sz
Rufinamide	Acts on inactivated voltage sensitive Na ⁺ channels	Adjunctive t/t of LGS (Lenaux Gestaut synd)
Stiripentol	Inhibits GABA transaminases → ↑GABA in brain	Dravet syndrome
Vigabatrin	V-Irreversible GABA transaminases inhibitor	DOC for infantile spasms a/w tuberous sclerosis complex
Topiramate	Weak CA (carbonic anhydrase) inhibitor	Broad spectrum anti-convulsant activity in maximal electroshock, PTZ induced/kindled Sz
Zonisamide	Blocks T-type Ca ⁺⁺ channels, activity dependent Na ⁺ channel	JME, LGS adjunctive role

CNS DRUGS/RECEPTORS

Serotonergic (5-HT) receptors & Drugs

5-HT-R	Agonist	Antagonist
Non-selective	LSD	-
Selective		
1A	DHE Ipsapirone Buspirone, gepirone (anxiolytic used in chronic anxiety)	
1B/1D	Sumatriptan (Used in acute attack of migraine)	
2A		Ketanserin, Ritanserin (Used in hypertension) Risperidone Cyproheptadine Methysergide
2A/2C	Clozapine (inverse agonist)	Clozapine
5HT ₃		MCP Ondansetron, Granisetron, Tropisetron (Used in chemotherapy induced vomiting) Alosetron (Used in IBS)
5HT ₄	Cisapride (Used in GERD) Renzapride, Tegaserod (partial agonist)	

→ **Sertraline, fluoxetine** : are 5-HT transport inhibitor useful in OCD, depression.

→ **Clozapine** have additional affinity for 5HT₅ & 5HT₆ receptors.

→ 5HT_{1B/1D} agonist **sumatriptan** is used in --- acute attack of migraine.

GABA Receptors

	Agonist	Antagonist
GABA-A	- Muscimol - Ethanol - GA: Propofol, BZD, barbiturates	- Bicuculline - Picrotoxin
GABA-B	Baclofen	Saclofen [mnemonic:-MBBS]

- GABA is the inhibitory neurotransmitter which acts by increasing Cl^- conductance.
- DMCM (β carboline) is inverse agonist at BZD site. Impedes GABA action.
- Flumazenil is competitive antagonist at BZD site.
- Picrotoxin blocks Cl^- channels non-competitively.
- BZD site. Impedes

BZD's

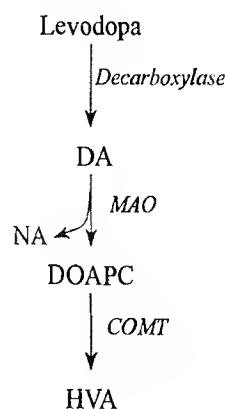
- BZD of preferred in elderly & those with liver d/s --- Lorazepam, oxazepam, temazepam
- BZD that do not produce active metabolites --- Lorazepam, oxazepam, zolpidem, triazolam, midazolam (MOLT)
- Longer acting BZD --- Flurazepam
- Shortest & fastest acting BZD --- Midazolam
- Anxiolytic and anti-depressants --- Alprazolam & Buspirone
- Diazepam generates active metabolites, has slow elimination, and tend to accumulate with regular use. Not preferred in elderly with liver d/s.

Dopaminergic Receptors

Receptor	Agonist	Antagonist
D_1	Dopamine Fenoldopam	- Bicuculline - Picrotoxin
D_2	Bromocriptine Pergolide, lergotriole Buspirone Apomorphine Cabergoline, Quinazoline	- MCP - CPZ - Domperidone - Haloperidol - Sulpiride, Benamide
D_2/D_3	Ropinirole, Pramipexole	

→ D_1 & D_5 ↑ cAMP while D_2 D_3 D_4 ↓ cAMP

Degradation of Levodopa



Peripheral decarboxylase inducer

PYRIDOXINE

- Abolishes the therapeutic effects of Levodopa
- ↓ on-off phenomena

Peripheral (extra-cerebral) decarboxylase inhibitor

CARBIDOPA, BENSERZIDE

- ↑ therapeutic effect of L-dopa by ↑ ing plasma $t_{1/2}$ (inhibits peripheral decarboxylation of L-dopa), ↓ es the dose requirement of L-dopa
- ↓ systemic toxicity of DA
- So, In t/t of Parkinsonism, L-dopa is combined with Carbidopa
- L-dopa + Carbidopa combination does not resolve involuntary movts, behavioural problems, postural hypotension.

Drugs for Parkinsonism

- DOC for drug induced parkinsonism --- Central anticholinergics (Benzhexol/ Triflu)
- Entacapone, Tolcapone :
Selective, potent & reversible COMT inhibitors

Alzheimer's D/s

- If patient is on Rivastigmine and develops depression TCA are contraindicated
- Donepezil is selective acetylcholinesterase inhibitor.
- Rivastigmine, Galantamine are other useful drugs.

Multiple Sclerosis

- For acute attack: Steroids (I/v pulse methyl prednisolone)
- To reduce recurrences and exacerbations:
 1. Interferon β -1a & 1b
 2. Glatiramer acetate (Resembles myelin basic protein)
- Drugs which slow the progression of disability in relapsing MS (Expanded disability status scale, EDSS)
 1. Mitoxantrone
 2. Cyclophosphamide
 3. Natalizumab : Mab directed against adhesion molecule α -4 integrin

Drugs in Stroke

- Storcit : Improves microcirculation in diffuse axonal injury.
- Dabigatran : Is most recent DTI (Direct thrombin inhibitor) used in prevention of stroke. It is a blood thinner recommended in non-valvular atrial fibrillation.
- Ximelagatran : Is also DTI (Direct thrombin inhibitor)

first member of its class. There is no antidote once acute bleeding develops d/to its use.

- **Idraparinux** : Is a LMW heparin with long $t_{1/2}$.

Other CNS Drugs

- **Ramelton** :

Orally active hypnotic drug used in t/t of **insomnia**. Acts on melatonin receptors - MT_1 and MT_2 . Exerts sleep promoting function without drug abuse liability.

- **Cysteamine** :

It depletes somatostatin. Useful in Huntington's disease

- **Reboxetine** : Newer SNRI antidepressant
- **Quetiapine** : Newer short acting atypical anti-psychotic.

OPHTHALMIC DRUGS

Brimonidine

- Clonidine congener.
- More selective α_2 action ($\alpha_2 \gg \alpha_1$)
- Ocular s/e are less. Used for both short term as well as long term control of IOT.
- Causes drowsiness.

Aproclonidine

- Polar clonidine congener used topically to ↓ IOT after glaucoma surgery (laser trabeculoplasty/ iridoplasty).
- ↓ aqueous flow in the ciliary body by selective α_2 action ($\alpha_2 \gg \alpha_1$)
- Ocular s/e: Lid retraction, lid dermatitis, itching, follicular conjunctivitis, dryness of mouth.

Brinzolamide

- Topically active reversible and non-competitive carbonic anhydrase inhibitor. Specific for **CA-II**
- More selective α_2 action ($\alpha_2 \gg \alpha_1$)
- ↓ aqueous production.

Ozurdex

- Intravitreal dexamethasone implant used as 0.7 mg injection.
- Used for macular edema following BRVO or CRVO and non-infectious posterior uveitis.
- *Latanoprost*
PGF $_2\alpha$ analog which ↓ IOT by facilitating aqueous drainage by ↑ ing uveosacral outflow. Used in glaucoma.

- *Isopropyl unoprostone*

Similar to latanoprost but it does not cause pigmentation.

CVS AND DRUGS

Digoxin/Digitalis

- Digitalis depresses nodal tissue (esp AV-node) and its effects mimic vagal effects e.g. ↓HR, ↑AV nodal delay etc. It is used to lower rapid ventricular rates in AF (when atrial rate 300-500/min)

- Digitalis has +ve inotropic & cardiac stimulant effect on all parts of heart except AV node.

- Indications of digitalis

1. CHF with hypertensive & coronary artery disease
2. Supraventricular arrhythmia (A.Fl & AF)
3. PSVT

- Digoxin is ineffective in --- Prevention of automatic atrial tachycardia

- Digitalis does not cause --- Vasodilatation

- **Digoxin toxicity**

- Inhibition of P-glycoprotein may play a role .
- Precipitated by --- Hypercalcemia, **hypokalemia**, hypomagnesemia, hypo/hyperthyroidism
- *Non-paroxysmal atrial tachycardia* is characteristic & ventricular bigemini is the m/c arrhythmia seen in digitalis toxicity
- Digitalis causes **2° Ht block**, **Mobitz type 1** (It does not cause --- Mobitz - II block & atrial flutter)

- **Digoxin is safe in liver d/s** because it is not metabolized by liver, But in renal d/s dose reduction is required. [However *Digitoxin* dose should be reduced in liver disease because **digitoxin is metabolized by liver. digitoxin is most lipid soluble cardiac glycoside**].

- Toxicity/ Serum concentration of digoxin is raised by ---Quinidine, verapamil, amiodarone, propafenone.

- S/c is better than i/v adrenaline

Epinephrine v/s Norepinephrine

Effect	Epinephrine(E)	Nor- Epinephrin (NE)
Metabolic	<ul style="list-style-type: none"> ↑ c-AMP ↑ Lipolysis ↑ glycogenolysis, ↑ glyconeogenesis ↓ insulin secretion, Hyperglycemia	↑ c-AMP
On slow i.v. / sc injection	↑ SBP ↓ DBP, ↑ mean BP & tachycardia	↑ All i.e. SBP, DBP, mean BP, & HR (Tachycardia)
On rapid i.v. injection	↑ SBP ↑ DBP fall in MBP	Reflex bradycardia
Local	Vasoconstrictor	Vasoconstrictor via α_1

Isoprenaline (Isoproterenol) causes (no α -action)

- ↑ SBP, ↓↓ DBP & mean BP ↓

After Adr administration: -

- if α - blocker (eg -ergotamine, prazosin) is given ---- ↓↓↓ in BP k/as *vasomotor reversal of Dale*
- if β - blocker e.g. propranolol is given ---- normalizⁿ of BP and it is k/as *vasomotor re-reversal of Dale*

Drugs reducing mainly

- Preload (venodilators): GTN, isosorbide nitrate
- Afterload (arterio-dilators): Hydralazine, CCB, minoxidil
- Both pre + afterload (mixed-dilators): Nitrates

Dobutamine

- Dobutamine consist of two isomers ---
(+) isomer is potent β_1 agonist & α_1 antagonist
(-) isomer is a potent α_1 agonist capable of causing significant vasoconstriction, when given alone.
- The only prominent action of clinical significance is increase in force of cardiac contraction and output without significant change in heart rate, BP and peripheral resistance (no vasodilatation or vasoconstriction).
- It has relatively selective β_1 action so no effect on bronchi.
- Dobutamine is a derivative of dopamine but no D_1 or D_2 action.

→ Receptors for NA, Adr. and DA(dopamine) all belongs to serpentine / seven pass receptor family

Nitrates

- Cause direct nonspecific smooth muscle relaxation (veins > arteries).
- Cause both preload as well as afterload reduction --- ↓ cardiac work & O_2 consumption. They favour redistribution of coronary flow to ischemic areas in angina patient.
- They dilate cutaneous v/s of face (flushing) and meningeal v/s (headache). Splanchnic and renal blood flow ↓.
- C/b used in : Angina pectoris, acute coronary syndrome, MI, CHF/ LVF, biliary colic, Achalasia cardia/ esophageal spasm, cyanide toxicity

- Penta Erythritol tetranitrate (PETN) longest acting
- M/A of nitrates → Nitrate gets denitrated in the smooth muscles to release NO → activates cGMP → dephosphorylates MLCK → relaxation occurs.
- All nitrates undergo extensive first pass metabolism except isosorbide mononitrate.
- Tolerance to hemodynamic and anti-ischemic effect develops soon if they are continuously present in the body. It is due to reduced ability to generate NO because of depletion of cellular SH-radicals.
- GTN is shortest acting nitrate.

Alpha -Agonists

- α_1 selective: Phenylephrine, methoxamine,
- $\alpha + \beta$ - agonist : Mephentermine. Used to prevent/treat hypotension induced by spinal anesthesia.

Alpha -blockers

- α -1B/1D receptors are found in blood vessels.
- Indoramine and urapidil are α -blocker anti-hypertensive agents.

Non-selective	Irreversible antagonist	Phenoxy-benzamine	Uses
	Reversible	Phentolamine Tolazoline	Used in clonidine withdrawal & cheese reaction.
α_1 blocker	$\alpha_{1A,1B,1D}$	Prazosine Trazocin Doxazocin	
	α_{1A}	Tamsulosin, Alfuzosin	Used in BPH (May cause floppy iris syndrome & retrograde ejaculation)
α_2 blocker		Yohimbine Idazoxine	

Beta-blockers

- o In HOCM, β -blockers improve cardiac output and relieve symptoms during exercise but are less useful in resting state.
 - o β -blockers are contraindicated in partial or complete heart block as they may cause bradycardia.
 - o β blockers with intrinsic sympathomimetic activity (partial agonist at β_1) [Mnemonic : CALPOL]
Celiprolol, alprenolol, acebutolol, pindolol, oxprenolol, - LOL
 - o β blockers with membrane stabilizing activity
Propranolol (max^m), metoprolol, labetalol, acebutolol, pindolol.
 - o Ad/e
 - β -blockers can precipitate CHF, life threatening attack of bronchial asthma.
 - Exacerbates variant (Prinzmetal's) angina due to unopposed coronary constriction.
 - Carbohydrate tolerance is impaired by propranolol but not by atenolol.
 - o Atenolol is cardioselective β_1 blocker. M/c β -blocker used for hypertension and angina
 - o Nebivolol is highly selective β_1 blocker which also acts as a NO donor.
 - o Both $\alpha + \beta$ blockers
 - Labetalol
 - Carvedilol ($\alpha_1 + \beta$ blocker, CVS stability, safe in glaucoma)
 - o β agonist + β blockers
 - Carteolol
 - Celiprolol
 - Bopindolol
 - o β agonist + K^+ channel blockers
 - Tilisolol
- Esmolol is ultra short acting β_1 blockers
→ Sotalol has non selective β blocking action

CALCIUM CHANNEL-BLOCKERS (CCB'S)

- o There are 3 types of calcium channels. Only the voltage sensitive L-type channels are blocked by CCBs.

	L-type	T-type	N-type
	(Long lasting current)	(Transient current)	(Neuronal)
Type	Slow	Fast	Medium
Location	SA, AV node	SA node, thalamus	Only on neurons
Blocked by	Nifedipine Diltiazem Verapamil	Flunarizine ethosuximide Mibefradil	ω -conotoxin

- o Nimodipine is cerebroselective CCB. It is most useful for prevention of cerebral vasospasm in patients with SAH

Clinical indications

- Prinzmetal angina : DOC is nifedipine > diltiazem > Verapamil
- In Arrhythmia : Verapamil > Diltiazem
- In Hypertension : Nifedipine and diltiazem > verapamil
- CCB with predominant peripheral action (maximum SM relaxation) : Nifedipine (used as tocolytics)

Remember

- In CHF verapamil and diltiazem are contraindicated. (Nicardipine & nifedipine may be useful.)
- In obstructive conditions (aortic stenosis and HOCM) CCB are contra-indicated.
- Coronary steal phenomena is seen with Dipyridamole, nifedipine and other CCBs, isoflurane, sodium nitroprusside
- Constipation is common with verapamil

ANTIARRHYTHMICS

Classification

Class	Actions	Drugs
I	Membrane stabilizers (Na^+ channel blockers)	
	a) Moderately ↓ dv/dt of phase 0	Quinidine, procainamide, disopropylamide, moricizine
	b) Little ↓ dv/dt of phase 0	<u>Lignocaine, Mexiletine, Phenytoin</u>
	c) Marked ↓ dv/dt of phase 0	Propafenone, flecainide
II	β-blockers	Propranolol, Esmolol, Sotalol
III	Agents widening AP (prolong repolarization and ERP)	Amiodarone, Bretylium, Dofetilide, Ibutilide
IV	CCB	<u>Verapamil, Diltiazem</u>
V	Others	Adenosine, Mg^{++} , K^+ , Digoxin, Atropine

M/m

- In WPW syndrome cardioversion is useful. Verapamil should not be used.
- Ibutilide is the best agent available for acute pharmacologic cardioversion of AF. Also called pharmacological defibrillator
- Valsalva manoeuvre is the first step for t/t in PSVT
- Acute symptomatic sinus bradycardia is treated by --- atropine (or isoprenaline), pacing in refractory cases
- Asymptomatic sinus bradycardia is seen in athletes d/to increased vagal tones.
- DOC for PSVT --- Adenosine

Inodilator

- Drugs which exhibit both direct inotropic + vasodilator properties.
- Examples are : Milrinone, amrinone
- **Milrinone** is a second generation phosphodiesterase inhibitor. It is the best inotrope used in RHF (right heart failure) and CHF.

GI DRUGS

Drugs in Irritable Bowel Syndrome (IBS)

For diarrhoea dominant IBS.

- Alosetron (5HT₃ antagonist)
- Mebeverine (Reserpine analog)
- **Fedotozine** (New κ opioid receptor antagonist)

For constipation dominant IBS.

- Lubiprostone (Cl⁻ channel activator)
- **Loxiglumide** (CCKI receptor antagonist)
- Tegaserod (5HT₄ agonists stimulates Ach & CGRP), prucalopride (5HT₄ agonists)
- Calcium polycarbophil

Laxatives

- Phenolphthalein has been withdrawn becoz of its cardiotoxicity.

DIURETICS

- Amiloride & Triamterine are inhibitors of renal epithelial Na⁺ channel.
- Frusemide causes negative water balance .
- Thiazides are first line drugs for HTN. Other uses are nephrogenic DI, d/to idiopathic hypercalciuria.
- Thiazides can cause erectile dysfunction/ impotence, hyperglycemia, hyperlipidemia, hyperuricemia, hypercalcemia, hypokalemic metabolic alkalosis. [Mnemonic: Thai ↑es GLUCAL and ↓ NaK]
- Diuretics such as thiazides and frusemides are contraindicated in patients with hyperuricemia (gout).
- Thiazides are contraindicated in a pt on lithium therapy, hypercalcemia.
- **Ticynafen (Indacrinone)** -- Diuretic safe in gout patient
- **Triemterene** is K⁺ sparing diuretic which blocks ENaC
- **Metirapone** blocks cortisol synthesis by inhibiting steroid 11 β -hydroxylase. This stimulates ACTH secretion.

	Thiazides	Frusemide	Acetazolamide	Spirolactone
Class	Medium efficacy	High ceiling/ loop	CA inhibitor (Sulfonamide derivative)	K ⁺ sparing
Site	Cortical diluting segment/ early DT	Loop	PT	Late DT & CD
Uses	HTN,	CHF, Acute LVF	Glaucoma, Absence seizure, ac. mountain sickness, idiopathic pulmonary edema	Cirrhotic/ nephrotic edema
Ad/e	↑Ca ⁺⁺ ↓Na ⁺ ↓K ⁺	↓K ⁺ ↓Ca ⁺⁺ ↓↓Mg ⁺⁺ Hyperuricemia, Acidosis	Metabolic ↓Na ⁺ ↓K ⁺	

DETRUSOR INSTABILITY

Drugs useful for t/t of overactive bladder/
Urge urinary incontinence

Detrusor m/s contracts in response to parasympathetic stimulation. Detrusor instability is d/to frequent contractions

of detrusor m/s. Anticholinergics are used to relax it/ to relieve bladder spasm.

- Oxybutynin (Anti-spasmodic on UB)
- Tolterodine (Vesico selective anti-muscarinic drug)
- Trospium (Non selective)
- Triptiramine
- Darifenacin and solifenacin (M_3 selective antagonist).
- Duloxetine: Dual NA +serotonin reuptake inhibitor.. Used in stress incontinence but NOT in detrusor instability.
- Anticholinergics are contraindicated in urinary retention.

ERECTILE DYSFUNCTION

- PDE-5 inhibitors (Sildenafil, tadalafil, vardenafil)
- PGE_1, E_2
- Alprostadil (c/b used transurethral)
- Inj. phentolamine
- Apomorphine
- Bremelanotide

◦ Bremelanotide

Used for erectile dysfunction. It was found useful in treating sexual dysfunction in both men (erectile dysfunction/ impotence) and women (sexual arousal disorders). It directly ↑es the sexual desire by acting on nervous system. It is also being tried in hemorrhagic shock & reperfusion injury.

HORMONAL/ENDOCRINAL DRUGS

Aromatase inhibitors

- Aminoglutethimide
- Cimetidine
- Letrozole, anastrozole
- Exemstane
- Aminoglutethimide

Androgen antagonists

- Cimetidine
- Spironolactone
- Progesterone
- Cyproterone acetate
- Cimetidine

Octreotide

Is the long acting potent analogue of somatostatin. It c/b used for acromegaly, secretory diarrhoea, a/w carcinoids and AIDS, islet cell tumours, esophageal varices.

Androgen receptor blocker

Flutamide, bicalutamide, nilutamides are useful in t/t of prostate cancer.

SERMS

(Selective Estrogen Receptor Modulator)

- Tamoxifen is used for t/t and prevention of estrogen receptor positive breast cancer.
- Raloxifene is agonist on estrogen receptors in some tissue (bone, liver, blood) and antagonistic on others (breast, endometrium). Used for t/t of osteoporosis, decreases risk of breast cancer, and protects against spine #

SERD

Fulvestrant is a selective estrogen receptor down regulator used in t/t of hormone receptor +ve breast cancer. It is safer, shorter acting, and more selective than SERM.

→ DHT is the most potent androgen

→ Finasteride is a 5α -reductase inhibitor which blocks $T \rightarrow DHT$ conversion. C/b used to relieve static BPH, male pattern baldness and prostate cancer. It can cause impotence.

→ DOC for BPH without affecting BP --- Tamsulosin

→ DES is an estrogen.

→ Prolonged administration of testosterone (e.g. in long term replacement therapy) in a man suppress the secretion of gonadotropins and may lead to acne, gynaecomastia, erythrocytosis, and azoospermia.

→ Prolonged administration of testosterone in a woman may lead to acne, hirsutism, clitoromegaly, and deepening of voice.

COAGULANTS AND ANTICOAGULANTS

Coagulants

- Type
- Vitamin K_1 (Phytonadione)
 - Vitamin K_2 (Menaquinone)
 - Vitamin K_3 (Menendione)

- **M/A** : Vitamin K1 is most widely used . Vit K is involved in the final step (γ -carboxylation of glutamate residue) of activation of clotting factors 2,7,9,10 as well as anti-clotting factors C and S

Anticoagulants

- **Oral anticoagulants**
(Prevent activation of factors 2,7,9,10)
 - Warfarin
 - Dicumarol, Coumarin
 - Phenindione

Indirect thrombin inhibitors

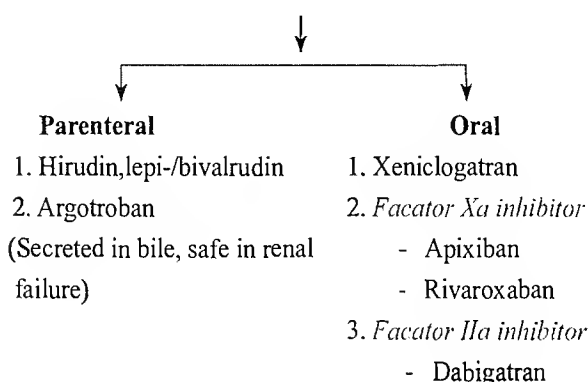
Heparin (i/v or s/c) : Strongest organic acid in the body. various forms are available

- Unfractionated : A~ of choice in pregnancy
- LMWH (Enxaparin, Dalteparin, and other -parins)
- Fondaparinux/ Idraparinux

Low Molecular Weight Heparin (LMWH)

- Depolymerized (fractionated) preparation of heparin.
- Molecular wt 3000-7000.
- Advantages over unfractionated heparin.
 - Less binding to cell and proteins.
 - Superior bioavailability
 - Longer plasma half-life
 - Lower incidence of thrombocytopenia and other Ad/E.
 - Given as s/c single daily dose , better compliance.
- Factor Xa assay is required to monitor effects of LMWH.
- Biochemical monitoring with aPTT does not require.

Direct thrombin inhibitors



- **Drotrecogin- α**
Recombinant APC (human activated protein C), used in severe sepsis. Inhibits coagulation by proteolytic inactivation of FVa & FVIIIa. Ad/e- bleeding.

- **Anticoagulants of choice in hypertensive pt.---** DTI's (Lepi/bivalrudin), Fondaparinux
- Apixaban, Rivaroxaban is oral factor X inhibitor
- Anti-platelet drugs are preferred in stroke.
- Warfarin is m/c drug used in pt with chronic atrial fibrillation.
- Warfarin (oral anticoagulant) effect is measured by INR. Target INR is 2-3 indicates good control. PT is m/c used method.

- If a patient develops bleeding d/to warfarin overdose FFP is the TOC but specific antidote of warfarin is vit K1
- Vitamin K₃ is contraindicated in patient with G-6-PD deficiency and in newborn as there are chances of kernicterus.
- 1 mg of vitamin K₁ i/m is given to all newborns at birth to prevent HDN (hemolytic d/s of newborn)
- Kinetics of warfarin changes from first order to zero order

- **Fibrinolytic/Thrombolytic drugs**
 - Streptokinase: Obtained from β hemolytic streptococci
 - Urokinase : From human urine
 - Reteplase/Alteplase : Recombinant
 - Tenecteplase: Longest acting
 - Altemprase: Metalloproteinase that degrades fibrin/FI
- EACA & Tranexemic acids are specific antidotes for overdose of fibrinolytic agents. Tranexamic acid competitively inhibits activation of plasminogen.
- Streptokinase** is an antigen, can cause hypersensitivity reaction and anaphylaxis (Thrombolytic agent with antigenic property).

ANTI-PLATELET DRUGS

- COX inhibitor : Aspirin
- TxA₂ synthase inhibitors: **Dazoxiben**
- ADPP2Y1C receptor antagonists: **Ticlopidine, Clopidogrel** (congener of ticlopidine)
- PDE inhibitor : Dipyridamole, Cilostazole (PDE-IIIi)
- **Glycoprotein inhibitors** Gp IIb/IIIa antagonists :
 - Abciximab
 - Eptifibatide, Tirofiban : Specific for GpIIb/IIIa
 - Xemilofiban: Oral drug, inhibits platelet aggregation
- Used in idiopathic myelofibrosis, essential thrombocytopenia, unstable angina.

HEMATINICS

- o Iron amino acid chelates have high bioavailability. Ferrous bisglycinate is a/w high rise of serum ferritin and lesser incidence of side effects.
- o Elemental iron is maximum in
 - ferrous fumarate (33%)
 - ferrous succinate (23%)
 - ferrous sulphate (20%) : Most frequently used salt
- o Iron chelators
 1. Parenteral : Desferrioxamine. Ad/e is growth retardation, cataract.
 2. Oral: Deferiprone, Pyridoxine, Hydrazine, HBED, Desferrothiocine
- o Drugs for Sick cell d/s
 1. *Hb production stimulating agent*-
Hydroxyurea, 5-Azacytidine, Butyrates
 2. *RBC HbS concentration reducing agent*:
DDAVP, CCB (Nifedipine & Verapamil)

HEMOPOIETIC GROWTH FACTORS

Cell	GF	Drug acting upon	Ind
RBCs	Erythropoietin	Epoetin, Darbopoietin	Anemia in CRF, with myelosuppressive drugs
WBCs	G-CSG	Filgrastim, Lenograstim	Neutropenia
	GM-CSF	Sargramostim, Molgramostim	Glaucoma
Platelets	Thrombopoietin	Romiplastim, Eltrombopag	ITP
	IL-11	Oprelvekin	Thrombocytopenia d/ to anticancer drugs

- o Romiplastin (Nplate) is thrombopoietin analogue . It decreases risk of bleeding.

ORAL HYPOGLYCEMIC AGENTS (OHA)

BIGUANIDES

OHA which lower glucose in type2 DM by ↓ing hepatic glucose output. Insulin secretion is unaffected so they are not secretagogues. Vitamin B₁₂ deficiency can occur with biguanides.

o *Metformin*

Is the DOC for t/t of DM in obese patients as it causes weight loss. It also causes vitamin B12 deficiency → megaloblastic anemia

o *Phenformin*

Causes lactic acidosis

INSULIN SECRETAGOGUES

They ↑insulin secretion from pancreas by interfering with K⁺ channels.

1. Sulfonylureas (SU)

Cause weight gain

Genera ^a	Drugs	Uses/ advantages	Ad/e
1st	Chlorpropamide	Longest acting	Cholestatic jaundice, clearance via K,L so C/ind in renal d/s.
	Tolbutamide		
	Tolazamide		
2nd	Glimepiride	Safe in renal d/s	
	Glipizide		
	Gliburide		
	Gliclazide	Antioxidant, prevents retinopathy, MI d/to anti-platelet action	

2. Non - Sulfonylureas

Rapaglenide and nataglinide are useful in patient with renal d/s or elderly.

o *Repaglinide*

Is a non-SU insulin stimulator, it induces insulin release.

☉ *Nateglinide*

Is a non-SU short acting OHA, limits post prandial glycemia in type 2 DM.

THIAZOLIDINEDIONES (EUGLYCEMICS)

1. Rosi- / Pioglitazone

↓ insulin resistance in m/s, adipose tissue & liver by ↑ing no. of GLUT. Act as **agonist** for nuclear PPAR γ receptor. It acts only in presence of insulin. Main ad/e is water retention & edema so not used in case of diastolic dysfunction. It is metabolized in liver by cytochrome p450 isoforms CYP2c8.

2. Troglitazone

Not used now d/to hepatotoxicity.

α -GLUCOSIDASE INHIBITORS

Acarbose and Miglitol

☉ **Acarbose**

Oligosaccharide which limits post prandial hyperglycemia by delaying absorption. It results in an insulin sparing action. It can be used in IDDM.

☉ **Miglitol** --- action is similar to acarbose

- Oral hypoglycemics that induce ovulation --- thiazolidinediones and metformin. Used in PCOS.
- Drugs causing hyperglycemia --- Glucagon, diazoxide, thiazides, phenytoins, somatostatin, streptozocin.
- Sorbinil, alconil, and Tolrestat are aldose reductase inhibitor. Can be used in diabetic neuropathy and retinopathy.

INCRETINS : Newer Drugs for Diabetes

☉ DPA -IV inhibitors

Vildagliptin and Sitagliptin are DPA -IV inhibitor

☉ GLP (Glucagon like peptide) inhibitors

GLP is naturally occurring insulin secretagogues found in duodenum, act as hypoglycemic factor. Recombinant GLP analogues . E.g. Exenatide, Liraglutide. Used for post prandial glycemia.

Exenatide

Synthetic GLP-1 receptor agonist effective in lowering Hb_{1AC}. Given s/c within 60 min before meal. Used in type 2 DM. Resistant to DPP-4.

Premilintide

Acts by suppressing glucagon release and delaying gastric emptying.

INSULINS

- ☉ Insulin Glargine and Insulin detemir are ultra long acting insulins while Insulin aspart and lisproinsulin are ultra short acting Insulins. [In general Insulins with the letter 's' are short acting while those with the letter 'L' are long acting.]
- ☉ Insulin acts by binding enzymatic receptor (tyrosine kinase receptor).
- ☉ Dose 0.8 - 1 U/Kg.

HYPERGLYCEMIC AGENTS

DIAZOXIDE

- ☉ K⁺ channel activator. (same K⁺ channels which are blocked by SU).
- ☉ Directly acting vasodilator. I/v bolus was used in the past for hypertensive emergencies but withdrawn d/to stroke and MI.
- ☉ ↓es insulin secretion and produces hyperglycemia.
- ☉ Clinically related to thiazide diuretics. Causes renal salt and water retention.

→ Drugs causing hyperglycemia --- Glucagon, diazoxide, thiazides, phenytoins, somatostatin, streptozocin.

STEROIDS

- ☉ Act by binding to intracellular receptors.
- ☉ Corticosteroids regulate hypothalamo-pituitary axis. Excess inhibits the synthesis of GC's synthesis.
- ☉ Hyperglycemia is an important ad/e. Anti-insulin effect

Indications of Corticosteroids

In SLE	In RA	In TB
1. TTP	1. Mononeuritis	1. Extensive d/s
2. Myo/peri-carditis	multiplex	2. TB-meningitis/ CNS TB
3. Hemolytic anemia	2. Pericarditis	3. Miliary TB
4. Alveolar hemorrhage	3. Systemic vasculitis	4. Pleurisy
5. Severe CNS symptoms (convulsions)	4. Scleritis	5. Pericarditis
6. Nephritis	5. Keratitis	6. Skin TB
		7. Polyserositis

- o Steroids are also indicated in:
 - Catecholamine resistant/profound shock
 - Meningococcal meningitis
 - o Steroids are NOT indicated in
 - Koch's abdomen
 - Progressive primary pulmonary TB
 - o Mineralocorticoid potency is maximum with aldosterone while glucocorticoid activity is maximum with dexamethasone. Systemic toxicity is least with prednisolone.
- | Properties | Max ^m | Min ^m |
|----------------------------|------------------|------------------|
| Mineralocorticoid activity | Aldosterone | - |
| Mineralo potency | Fludrocortisone | - |
| Glucoc activity | Dexa | Cortisone |
| Glucoc potency | Beta | Cortisone |
- o Anti-inflammatory action of cortisol is d/t to inhibition of synthesis /release of leukotrienes.
 - o Excess glucocorticoids cause → muscle wasting and myopathy → ↑ weakness
 - o GC's ↑ secretion of gastric acid and pepsin so aggravate peptic ulcer
 - o Patients of Addison's d/s suffer from apathy, depression and occasionally psychosis.
 - o Exogenous steroids are given in CAH to suppress ACTH secretion.
 - o GC's on prolonged use can lead to Cushing's syndrome, hyperglycemia, osteoporosis, cataract (prolonged systemic steroid use), glaucoma (on chronic topical use), ↑ susceptibility to infections, and delayed wound healing.
 - o Corticosteroids prevent intestinal absorption of calcium → hypocalcemia.
 - o GC's promote glycogen deposition in liver by inducing hepatic glycogen and promoting gluconeogenesis.
 - o GC's restrict capillary permeability, maintain tone of

arterioles and myocardial contractility,

- o *Permissive action* in development of HTN by:

- Analgesic effect of kytorphin
- Induction of dALA
- CA (catecholamines) action on heart.

→ GC's cause LEB low i.e. lymphopenia, eosinopenia, basopenia (but leucocytosis and neutrophilia)

→ GC causes marked destruction of lymphoid cells, so lytic response is shown by malignant lymphatic cells. So used in malignant lymphoma

INDICATIONS OF

Indications of IV Immunoglobulins

- o Primary humoral immunodeficiencies (for prophylaxis)
 - o **Kawasaki disease** (mucocutaneous lymphnode syndrome)
 - o ITP
 - o Bone marrow transplantation
 - o Chronic B-cell lymphocytic leukemia
 - o Pediatric HIV-1 infection
 - o GBS and chronic demyelinating polyneuropathy
 - o GVHD
 - o Common variable immunodeficiency
 - o Myasthenia gravis
 - o Multiple sclerosis
- (IGs are not known to cause fetal harm during pregnancy)

Neostigmine

- o Acute congestive glaucoma
- o Myasthenia gravis
- o Post. operative paralytic ileus/urinary retention
- o Cobra bite
- o Belladonna (Datura) : Physostigmine is preferred because it crosses BBB.
- o Post operative decurarization

Methotrexate

- o Rheumatoid arthritis (1st line DMARD)
- o Psoriasis
- o Ankylosing spondylitis (for peripheral involvement only)

Co-trimoxazole

- o Upper and lower RTI
- o Atypical pneumonia (Pneumocystis carinii)
- o Whipple's d/s

- Dysentery
- UTI
- Shigellosis
- Enteric fever
- Shigellosis

Ergot derivatives

- Maximum α -blocking property --- DHE
- Vasoconstriction and emesis are seen with --- Ergotamine
- 5-HT blocker --- Methysergide
- Oxytocic --- Ergometrine (ergonovine)

Selective β_2 agonists

- Used in asthma
 - Salbutamol (albuterol), orciprenaline, terbutaline
 - Salmeterol & formoterol (Newer long acting inhalational agent useful in chronic asthma)
- Tocolytics (uterine relaxants)
 - Ritodrine
 - Terbutaline
- β_2 agonists are also useful in hyperkalemic periodic paralysis.
- Salmeterol is longest acting β_2 agonist

Thalidomide

- Used for limited indications
- Teratogenic drug : Known to produce phocomelia in fetuses
- Clinical Uses : AIDS related recurrent aphthous ulcers/ wasting syndrome, resistant forms of multiple myeloma, GVHD, RA, AS, Behcet's syndrome, Crohn's d/s, ENL
- Ad/e : Constipation, peripheral neuropathy, sedation
- Reduces TNF α production.

Drugs used for t/t of post-menopausal Osteoporosis

- Anti-resorptive agents :
 - Biphosphonates (Alendronate, risedronate)
- Calcium, Vitamin D, estrogen supplementation
- SERM (Raloxifene)
- Bone anabolic agents e.g. Teriparatide (rPTH)
- Strontium ranelate (dual action bone agents DABAs)

COX & LOX PATHWAY

Cyclooxygenase [COX]

- COX has an inhibitory action on cell differentiation
- Exists in two isoforms COX-1 and COX-2
 - COX-1 is constitutively expressed and is active in most cells
 - COX-2 is normally present in minute amount, but at certain sites (kidney & brain) it is expressed constitutively. COX-2 is inducible by cytokines/ growth factors especially in inflamed tissues.
- Aspirin (Salicylates) is the most potent and irreversible inhibitor of COX and also TXA₂-synthase. Even a single dose can impair hemostasis (platelet function) for 5-7 days. Aspirin acetylates platelet COX irreversibly.
- Most NSAIDs are non-selective COX inhibitors. NSAIDs (e.g., aspirin, ibuprofen, indomethacin) inhibit both the COX-1 and COX-2 enzymes.
- Selective COX-2 inhibitors:
 - Rofecoxib (most selective), celecoxib, etoricoxib, valdecoxib, meloxicam and nabumetone are long acting reversible inhibitor of COX-2. They do not induce the gastric inflammation & have no adverse effects on platelet aggregation. Coxibs are withdrawn from market d/to ↑ incidence of MI.
 - Aspirin (salicylates) is irreversible COX inhibitor while other NSAIDs are competitive and reversible inhibitors.
 - Acetaminophen is inhibitor of COX isoenzyme & has additional COX-3 inhibition (present in CNS)
 - Zileuton inhibits 5-lipoxygenase (LOX)
 - Glucocorticoids inhibit membrane phospholipid by stimulation of annexins/ lipocortins (which are inhibitor of phospholipase A₂). They also inhibit induction of COX-2

Prostaglandins

- Dianoprostone--- Used for augmentation of labour
- Misoprostol --- Used for induction of labour & inducing abortion in 1st few months of pregnancy.
- Misoprostol, reoprostil, enprostil--- Used for healing of peptic ulcer
- Alprostadil --- Used to maintain patency of ductus arteriosus.
- The cyclooxygenase (COX) enzymes (referred to as prostaglandin synthases in the mouse) catalyze the conversion of arachidonic acid → prostaglandin H₂ (PGH₂), which is the rate-limiting step in synthesis of biologically active prostaglandins (and thromboxane A₂).



Thromboxane A_2 , Prostacyclin, Prostaglandins (A, D, E_1, E_2, F, I_2)

PG	Tx- A_2 (Thromboxane A_2)	PGD ₂	PGE ₁	PGE ₂	PGF _{2α}	PGI ₂ (Prostacyclin)
Vasodilatation	- (Vasoconstrict ⁿ)	-	+	+	+	+
				(but vasoconstrict ⁿ of large veins)		
Bronchodilator	- (Bronchoconstrict ⁿ)	-	+	+++	-	+
Gastric mucosa			Protective	Protective	-	Weak action
Other effect	Platelet aggregation Hemostatic, Release reaction	Anaphylaxis		Cx ripening, Uterine contractions, Pyrogenic	Uterine contractions	↓Platelet aggregation, ↓Platelet release Anti-inflammatory
Major use	Promotes thrombus formation		Asthma, To maintain patency of DA, Ulcer	Induction/ augmentation of labour, MTP/ abortifacient, Asthma	Oxytocic, Uterine atony/ PPH	Prevents thrombus formation in health
Acts on receptor	TP-receptor	DP	EP	EP (via c-AMP)	FP (via c-GMP)	IP
Analogues & uses			1. Misoprostol, 2. Alprostadil (to maintain PDA)	Enprostil, Dianoprost	Carboprost, Latanoprost (used in wide ∠ glaucoma)	1. Cicaprost, 2. Epoprostenol c/b used in hemodialysis to prevent platelet damage

DRUGS DURING SURGERY

- Prostacyclin and Thromboxane A_2 are mutually antagonistic.
- PG- D_2 , Tx A_2 , LT, PG- F_2 are potent bronchoconstrictors
Largest amt. of PG's are seen in seminal fluid.
- Prostaglandins in general are vasodilator (antihypertensive)
↑GFR, causes diuresis, natriuresis & kaliuresis, purgative,
↑Renal blood flow (RBF)
- PG- D_2 , Tx A_2 , LT, PG- F_2 are potent bronchoconstrictors
(mnemonic : DALF)
- PG- E_2 & PGI₂ maintain the patency of ductus arteriosus during fetal life (indomethacin and aspirin induces closure of it)
- PGE₂ > PGE₁, PGI₂, PGA₁ are ulcero-protective (not F_{2α})
- PGE₁ & E₂ has been used for T/t of asthma

To produce deliberate hypotension

- Trimethopran : Ultra-short acting ganglion blocker (N_N)
- Arphonad
- Fenoldopam,
- Adenosine and alprostadil,

Drugs withhold during surgery

- Antihypertensives
- Anti-coagulants (Clopidogrel, warfarin)
- Oral hypoglycemics

- NSAIDs, LMWH, Ecosporin can be contd/given during surgery.
- Clopidogrel is hold 5 days before surgery.

IMMUNOSUPPRESSIVE AND ANTI NEOPLASTIC DRUGS / CHEMOTHERAPY DRUGS

- o *Mycophenolate mofetil* is a prodrug used in transplant rejection. It should not be used along with azathioprine. M/c ad/e is GI upset.
- o *Gefitinib* is a selective EGFR tyrosine kinase inhibitor (inhibitor of HER1/ Erb1).
- o *Lapatinib* is a inhibitor of HER1/HER2 tyrosine kinase (EGFR2). It is used in t/t resistant or triple +ve (ER + EGFR+HER2) breast cancer.
- o M/c cause of dose limitation of a cytotoxic/ chemotherapeutic drug is --- bone marrow depression.
[Anticancer drugs are given in detail in onco section]

NEWER DRUGS IN T/T OF ----

- | | |
|-------------|---|
| Hepatitis B | ---- Nucleoside RT/ DNA p inhibitors entecavir, telbivudine, tenofovir, clevudine, emtricitabine are in clinical development |
| Chronic HCV | --- Pegylated interferons, Viroline under clinical development |
| HSV | --- Resiquimod (<i>topical immunomodulator</i>) under clinical development |
| Rhinovirus | --- Pleconaril (<i>capsid binder</i>) under clinical development |
| CMV | --- Maribavir (<i>DNA synthesis inhibitor</i>) under clinical development |
| CML | ---- Imatinib mesylate |
| Obesity | ---- Sibutramine (inhibits the reuptake of NA & 5-HT),

Orlistat (acts by inhibiting intestinal lipase, also inhibits progression of DM2) |
- o **Telbivudine** is β -L enantiomer of thymidine & is potent inhibitor of HBV DNA polymerase
 - o **Entecavir** is Guanosine analogue that inhibits HBV DNA polymerase + also useful against HIV. Approved for t/t of chronic hepatitis B in adults.

MONOCLONAL ANTIBODIES (MABS)

Monoclonal antibody (Mab)	M/A	Mechanism/ Use
Belimumab	B-lymphocyte stimulator-specific inhibitor	For active SLE
Bevacizumab	VEGF	Metastatic colorectal cancer, combined with 5-FU
Ipilimumab	CTLA-4 blocking Mab	Unresectable /metastatic melanoma
Omalizumab	Anti-IgE Mab	Resistant asthma patient
Pavilizumab		Prevention of RSV (bronchiolitis) in high risk infants
Ranibizumab	VEGF inhibitor	Macular edema, Neovascular Age related MD
Rituximab	Anti-CD20	Non-Hodgkin's lymphoma
Alemtumab	Anti-CD52	Low grade lymphoma & CLL
Zemtumab	Anti-CD33	CD33+ve AML
Donesumab	RANK ligand inhibitor mab	Mimics the activity of osteoprotegerin. Used in osteoporosis

IMPORTANT/NEW DRUGS

Drug	Class	Mechanism/ Use
Aprepitant	Substance P antagonist	Blocks NK1 receptor, anti-emetic
Ezetimibe	Hypolipidemic	Inhibits intestinal cholesterol & phytosterols absorption

Drug	Class	Mechanism/ Use
Eptifibatide &	Peptide	Platelet glycoprotein GPIIb / IIIa inhibitor
Tirofiban	Non-peptide	GPIIb/ IIIa antagonist
Ticagrelor		Reversible binding ADP-R antagonist
Tigecycline	Antibiotic	First glycylcycline to with activity against Gram-negative bacteria
Bosentan	Endothelin receptor antagonist	Acts on ETa & ETb receptors. Used for primary pulmonary HTN to ↓ PAP
Brimonidine	Clonidine congener	More α_2 selective & lipophilic
Fosfomycin,		Useful in UTI
Ginkgolide-B/ Alprazolam /triazolam	PAF antagonist	
Glycopril, Alatriopril		ACE inhibitor + stimulates ANP
Indoramin & Urapidil	α_1 blocker	Inhibits proliferation of activated lymphocytes in RA
Leflunomide	Immuno-modulator	Pyrimidine synthesis inhibitor used in RA
Anakinra	IL-1 antagonist	Recombinant drug used in RA
Methisazone		Inhibits in vitro replication of small pox ds DNA (variola) and vaccinia virus
Ranolazine	LC3-KAT inhibitor	Metabolic modifiers used in resistant chronic angina
Trimetazidine	Anti-angina	Acts by non-hemodynamic mechanisms
Nesiritide	Natriuretic peptide	Human recombinant B-type natriuretic peptide useful in t/t of acute heart failure

Drug	Class	Mechanism/ Use
Tegaserod	5-HT ₄ partial agonist	Acts as antiemetic and purgative by stimulation of Ach & CGRP, in IBS
Infliximab, Etanercept	Anti-TNF α Antibody	Used in resistant Crohn's d/s, RA, Ankylosing spondylitis & psoriasis
Erlotinib	Tyrosine kinase inhibitor, acts on EGFR	Used in Non small cell lung cancers., pancreatic cancer etc
Tryptamine	M ₂ antagonist	Used in vagal bradycardia
Levosimendan	Inodilator	↑ sensitivity of troponin C to intracellular Ca ⁺⁺ , useful in acute heart failure
Temozolomide	Oral alkylating agent	
Losartan	AT ₁ -R AII blocker	Competitive blocker of AII more selective for AT ₁ receptors
Olmesartan	New AT-R blocker	AT ₁ -R AII blocker
Duphaston	Retro-progesterone	Immunomodulator, ↑ Th ₂ levels. Used in recurrent/ threatened abortion

IMPORTANT POINTS FROM RECENT EXAMS

- Artificial RBCs / blood substitutes — Per fluoro carbons (Fusol-DA)
- Artificial tears — methyl cellulose drops.
- Artificial cement substance — hydroxy-apatite

- **Automatism** is a feature of complex partial seizures. **Automation** is seen with - Barbiturates poisoning. treated by picrotoxin.
- Auto induction** is seen with-Barbiturates. carbamazepine Rmp, phenylbutazone
- Auto inhibition** is seen with - Allopurinol
- Pyridoxine should be given with - INH, cycloserine, hydralazine & OCPs induced mental symptoms.
- Meprobamate is a metabolite of Carisoprodol
- **Buspiron** is anxiolytic drug without much sedative,

hypnotic or euphoric effect. Useful in generalised anxiety. Not suitable for acute anxiety because it takes week to establish its effects.

- Infliximab c/b used for RA + pulmonary fibrosis.
- Anti TNF α drugs c/b used for RA + HBV/HCV/pulmonary fibrosis.
- Erythromycin binds to motilin receptors and enhance GI motility.
- Allopurinol is used in t/t of chronic gout.
- Trientine is used in t/t of Wilson's d/s for mild/moderate hepatic decompensation.
- Drugs used in t/t of juvenile myoclonic epilepsy --- Valproate is DOC. Other drugs are topiramate, zonisamide and lamotrigine.
- Mitomycin C is topical drug used for tracheal and subglottic stenosis.
- Drug resistance in MRSA is d/to --- Change in penicillin binding receptors
- Drugs for heparin induced thrombocytopenia --- Lepirudin, Danaparoid, Argatroban
- Amphotericin B toxicity c/b lowered by using liposomal delivery systems.
- Adrenaline is used for immediate t/t of anaphylaxis.
- Safe dose of isotretinoin : 0.5- 1 mg/kg/d.
- Ramelteon bioavailability is <2%.

SOME IMP. NEGATIVE POINTS

Drugs not useful in / ineffective

Vs Anaerobes → Aminoglycoside, carbenicillin

Vs E coli, klebsiella,

H. Influenzae → Penicillin V

Vs Pneumococci → Fluoroquinolones

Vs Pseudomonas, strepto → Tetracycline

- Drug which does NOT interfere with warfarin metabolism --- Corticosteroid.
- Octreotide is NOT useful in treatment of --- Glioma.
- Peripheral neuropathy NOT seen with --- Lamivudine, zidovudine
- Primaquine is Not used as --- Anti sporozoite or Blood schizonticide
- All 1st line Antitubercular drugs are bactericidal/E--- Ethambutol
- Antacids do NOT decrease the bioavailability of --- Erythromycin.

- NOT a hepatic microsomal enzyme inducer --- Tolbutamide
- Mebendazole is NOT used in T/t of --- Strongyloides, Schistosomiasis
- Albendazole is NOT used in T/t of --- Schistosomiasis
- NOT included in pharmacogenetics --- ADA deficiency
- t $\frac{1}{2}$ of a drugs does NOT tell about --- Safety margin of drugs.
- NOT an indirectly acting sympathomimetic --- Dopamine.
- Busulphan does NOT causes --- Cardiotoxicity
- Methemoglobinemia is NOT caused by --- Phenytoin
- Dobutamine does NOT exert its effect by --- Dopamine receptors
- Dopamine does NOT have --- β_2 Activity
- Domperidone --- is NOT useful in motion sickness
- Azithromycin --- is NOT useful in pseudomonas infection
- Pseudomembranous colitis is NOT caused by --- Aminoglycosides
- NOT a side effects of fluoxetine --- Drowsiness
- Pyridoxine should not be given with --- Cyclosporine (It is given alongwith cycloserine)
- Cholestatic jaundice is NOT common with --- INH
- Liver toxicity is NOT seen with --- Streptomycin, Ethambutol.
- NOT a risk factor for digitalis toxicity --- Hyperkalemia.
- NOT prodrugs --- Phenobarbitone, lisinopril, captopril
- In G6PD deficient hemolysis is NOT precipitated by --- Estrogen
- Cyclosporine does NOT cause --- Dose related hepatotoxicity
- NOT a THFR inhibitor --- Cytosine arabinoside (cytarabine)
- Megaloblastic anemia is NOT seen with --- primaquine
- Peripheral neuropathy is NOT caused by --- Methotrexate
- Morphine is not used for pain arising from --- biliary colic, diverticulitis, pancreatitis (undiagnosed abd. pain)
- NOT an opioid agonist --- Ketamine
- Drug NOT used for AIDS --- Fanciclovir, anti TNF α
- Thalidomide is NOT used in --- HIV associated peripheral neuropathy
- NOT an adverse effect of Thalidomide --- Diarrhoea
- Drug NOT used in narrow angle glaucoma --- Duloxetine
- Drug NOT used in prophylaxis of migraine --- Sumatriptan
- Oligospermia is NOT an adverse effect of ---

Penicillamine

- NOT true of flumazenil --- It c/b used in barbiturate poisoning as it blocks GABA
- Drug NOT used for visceral Leishmaniasis --- Hydroxy-chloroquine
- Nitrates can NOT be used for --- Renal colic
- NOT a mechanism to convert benzopyridine to carcinogen --- Epoxidation.
- NOT true about ACE inhibitors --- Omission of prior diuretic dose reduces the risk of postural hypotension.
- ACE inhibitor which is NOT a prodrug --- Captopril, lisinopril.
- Voriconazole is NOT used for --- Mucormycosis
- Drug NOT used in t/t of juvenile myoclonic epilepsy --- Carbamazepine
- MAO inhibitors should NOT be used with --- Pethidine
- Serotonin syndrome is NOT caused by --- RIMAS (Reversible inhibitor of MAO)
- Hirsutism is NOT seen with the use of --- Flutamide
- NOT true of penicillin binding proteins --- Only mode of resistance for staphylococcus
- NOT a mechanism of action of theophylline --- β_2 agonism.
- NOT used as an antidote in amitriptyline overdose --- Atropine
- Tolerance to opioids does NOT develop for --- Miosis
- Drug which is NOT used to treat alcohol dependence --- Flumazenil
- NOT an action of muscarinic antagonist--- Miosis and prolonged AV conduction
- NOT seen in digoxin toxicity --- Regularisation of AF
- Drug which is NOT used to modify the course of d/s in diabetic retinopathy --- Tamoxifen
- NOT a phase 1 reaction --- Conjugation.
- Interstitial nephritis is NOT caused by --- INH.
- Monitoring of serum levels is NOT needed for--- Warfarin.
- Antibiotic which is NOT bactericidal --- Tigecycline.
- Thalidomide does NOT cause --- Myocarditis.
- Octreotide is NOT useful in t/t of --- Glioma.
- Drug NOT useful against MRSA --- Cefaclor
- Which does NOT cause hypoglycemia --- Acarbose.
- Methotrexate is NOT used in --- Sick cell anemia.
- Drug which does NOT worsen angina --- Oxyfedrine
- Tamoxifen use for breast cancer do NOT cause --- Carcinoma in contralateral breast.
- Naloxone does NOT cause --- Seizures.

SOME NEWER DRUGS

Drug	Class or M/A	Mechanism/ Use
Dexmedetomidine	Centrally acting Selective α_2 A agonist	Used for preanaesthetic medication/ sedation in ICU
Nesiritide	Recombinant BNP (Brain natriuretic peptide)	Vasodilator secreted from left ventricle
Rupatidine		Antihistaminic + PAF antagonist
Trimetazidine	Novel antianginal dg	acts by non hemodynamic mechanisms.
Ivabradine	\downarrow HR by \downarrow ing currents in SAN	Chronic stable angina
Diacerine	IL-1 antagonist	DMRD in osteoarthritis
Ixabepilone		Resistant breast cancer, used with capecitabine
Tolazoline	α blocker	Used during angiography to relieve vasospasm. Systemic + pulmonary vasodilator
Duloxetine	Centrally acting drug	Stress urinary incontinence
Denileukin deftitox		Advanced cutaneous T cell lymphoma
Donesumab	RANK ligand inhibitor mab	Mimics the activity of osteoprotegerin. Used in osteoporosis
Ramelteon	Orally active hypnotic	MT-1 & MT-2 receptor agonist
Rosuvastatin		Latest and most potent statin
Lacidipine		A highly vaso selective newer DHP anti hypertensive suitable for OD administration
Mecamylamine	Nicotine antagonist	block the rewarding effects of nicotine
Modafinil		Non-amphetamine compound used for t/t of narcolepsy
Phenazopyridine	\downarrow Burning micturition	Urinary analgesic
Tizanidine	central α_2 agonist	clonidine congener

GENERAL FORENSIC

Sections of IPC (Indian penal code)

Punishment is mentioned in bracket.

- S. 8 --- Related to gender
- S. 82 --- Any act done by a child < 7 years of age is not an offence.
- S. 84 --- Deals with criminal responsibility and insanity
- S. 147 --- Punishment for rioting
- S. 191 --- Perjury (giving false evidence). Witness becomes hostile.
- S. 192 --- Fabricating false evidence
- S. 193 --- Witness is liable to be prosecuted for perjury / punishment for false evidence (7 years)
- S. 197 --- Issuing or signing false certificate is punishable (7 yr)
- S. 228A --- Disclosure of identity of the victim of certain offences, like rape.
- S. 299 --- Culpable homicide not amounting to murder.
- S. 300 --- Murder
- S. 302 --- Punishment of murder (death/life term)
- S. 304 --- Punishment for culpable homicide not amounting to murder
- S. 304 A --- Deals with death d/to criminal negligence/ proved case of medical negligence (2yrs)
- S. 304 B --- Deals with dowry death.
- S. 306 --- Abetment to suicide (10 yrs)
- S. 307 --- Attempt to murder (death/10 yr)
- S. 308 --- Attempt to commit culpable homicide(3/7y)
- S. 309 --- Attempt to commit suicide (1yr)
- S. 319 --- Hurt & its definition
- S. 320 --- Deals with greivous hurt.
- S. 323 --- Punishment for voluntary hurt (>1 yr)
- S. 324 --- Punishment for hurt with dangerous weapon like shooting,stabing,cutting etc. (3 yr)
- S. 325 --- Punishment for greivous hurt (7yrs)
- S. 326 --- Punishment for greivous hurt (10 yrs)

- S. 336 --- Deals with rash negligence but no harm (If a drunk doctor conducts safe delivery)
- S. 340 --- Wrongful confinement
- S. 351 --- Deals with assault/abduction
- S. 354 --- Deals with assault to outrage the modesty of women
- S.375 --- Defines rape
- S.376 --- Punishment of rape
- S.377 --- Unnatural sexual offences (sodomy etc.)
- S.497 --- Adultery
- S.498A --- Cruelity to women by her husband/relative

It is very difficult to remember all the IPCs at a time . It is advised to PG aspirants to remember the IPCs in groups. e.g. IPCs related to injury/hurt are b/w 319 to 324, which you can choose easily from the options with wide variations

- Acts dealing with medical negligence are 37, 312 IPC
- Criminal procedure code (CPC) section 174 deals with police inquest while 176 deals with magistrate's inquest.
- Acc/to Indian evidence act sec 32 deals with dying declaration.

Sections of CrPC (Criminal Penal code)

CrPC was enacted in India in 1973 by law comission of India. It came into force in 1994.

- 2c --- Cognisable offense
- 8c --- Punishment of narcotic & substance abuse
- 26b --- Offence triable under court-order.

Offense

- Cognizable offense signifies arrest without warrant
- Punishment for dowry death is 5 years imprisonment + Rs. 15,000 fine.

Importance of age for medicolegal purpose

- Any act which is done by a child <7 year of age is NOT an offense. Age of criminal responsibility in India is 7 yrs.
- A person is presumed dead as per law if not seen or heard for by his/ her near and dear ones for----7 years
- A child below 14 years can not be employed to work in any factory/ risky job. Under labour act a boy or girl <14 is prohibited from any form of labour activity. Any child of <18 yr can not be employed in hazardous work.
- Sexual intercourse by a man with a girl < 15 years if she is his own wife or with any other girl < 16 years even with her consent is considered as rape.
- A person attains majority on completion of 18 years (or 21 years when under guardianship of court).
- A person above 18 years of age can give valid consent.
- Maximum period of observation for proving insanity — 30 days

Juvenile Delinquency act 1960

- As per existing law in the country, upper age limit of a boy & girl is 18 to be called as juvenile.
- So as per Indian law a boy <16 & a girl <18 both are juvenile.

Consent

- Legal age of consent is 18 yrs.
- A person below 12 yrs cannot give valid consent to suffer any harm, (Sec. 89, IPC).
- In emergency, law implies consent. (A person involved in accident which may necessitate amputation or a head injury case requiring urgent decompression)
- In criminal cases the victim cannot be examined without his/her consent.

- Death should be registered within 7 days and birth within 14 days.
- For issuing death certificate no charges or fee is entitled for RMP.
- Issuing or signing false certificate is punishable under S. 197 IPC.

Imp. Rules / Definitions

- **Mc Naughten's rule. Curren's Rule and Durham Rule** deal with criminal responsibility of insane (S 84).
- **Mc Naughten's rule**----A person is not responsible for his crime if he is not of sound mind.
- **Irresistible Impulse Test** : "An accused person is not criminally responsible, even if he knows the nature and

quality of his act and knows that it wrong, if he is incapable of restraining himself from committing the act, because the free agency of his will has been destroyed by mental disease".

- **Res. ipsa loquitur** : Means thing or fact speaks for itself.
- **Res judicata** : If a question of negligence against a doctor has already been decided by a court in a dispute between the doctor and his patient, the patient will not be allowed to contest the same questions in another proceeding b/w himself and the doctor. (section 300, Cr. P.C.)
- **Vicarious liability** - an employer is not only responsible for his own negligence but also for the negligence of his employees.
- **Novus actus interveniens** : A person is responsible not only for his actions, but also for the logical consequences of those actions.
- **Perjury** - giving willful false evidence by a witness while under oath (IPC 191 defines it, punishment in 193).
- **Holograph will**-- Will written by a testator in his own handwriting
- **Testamentary capacity**-- Is the mental ability of a person to make a valid will
- **Subpoenal summon** --- Is the document impelling the attendance of witness in court under penalty
- **Conduct money** --- Refers to fee offered or given to witness to cover the expenses for attending court in civil case. it is paid by govt. However in criminal case, no fee is paid and witness has to attend the court). Paid by govt.
- **Plaintiff** --- Refers to a person who has been harmed in some way & is seeking compensation.

- *Casper's dictum (old rule of thumb) is used for ascertaining time since death. 1 week of putrefaction in air is equivalent to 2 weeks in water, which is equal to 8 weeks buried in soil, at same environmental temperature*
- *Corpus Delicti refers to -- Body of offense or facts of crime*
- *Dry submarine means -- Tying of a plastic bag over the ears in custodial torture injuries.*
- *Privileged communication signifies communication b/w doctor and concerned authority*

Inquest (Judicial Inquiry)

- **Magistrate's inquest** (inquiry by magistrate) is conducted in the following cases:
 1. Death of a convict in the jail/ lock up
 2. Death of a person in police custody
 3. Death as a result of police shooting

4. Dowry death, Exhumation death

5. Death in a mental hospital

- Police inquest is the m/c type of inquest in India. Investigating officer is above the level of head constable.
- Coroner's inquest is conducted only in Mumbai by 1st class JM. It is the only court of inquiry.

- Appeal against consumer redressal can be filed in 'District Forum' (State commission).

- *Leading questions are permitted only in cross examination.*
- *Dying deposition is recorded by magistrate & it carries more weight than dying declaration in court of law.*
- *Medicolegal autopsy requires the permission of magistrate & police both.*
- *In civil negligence onus of proof lies on patient.*
- *In India inquest is NOT carried out by a doctor*
- *For exhumation order is passed by chief judicial magistrate*
- *Juvenile court is presided over by 1st class woman magistrate*

Exhumation

- Order is passed by **magistrate**/coroner.
- Done in early morning. Legally no time limit.
- Lawful digging out of a buried body from the grave for the purpose of identification or determination of cause of death. Can be conducted in natural day light, under the supervision of medical officer & magistrate.

Witness

Common witness:

One who actually saw or heard (first hand knowledge rule), but cannot draw any inference.

Expert witness:

One who is skilled or trained in scientific skills & is capable of drawing conclusion eg firearm expert, chemical expert, fingerprint, handwriting experts. etc.

Medical certificate is simplest form of documentary evidence. Issued by doctor & no fee is charged for it.

Oral evidence or testimony

Mental ability of a person to make a valid will. It is more important than documentary evidence because it allow cross examination to determine its accuracy.

Exception

- Dying declaration
- Deposition of medical witness taken in lower court.
- Report of scientific expert.

IDENTIFICATION

FINGERPRINTING

- Also K/as **dactylography**/ Galton system or dermatoglyphics
- Finger printing bureau was first established in Kolkata (in India)
- M/c pattern is **loops** (67%) > whorls (25%) and composite patterns (1-2%) are least common
- Dactylography is the most reliable/ best method of identification of an individual. Fingerprint pattern is different even in identical twins (**Quetelet's rule**). Fingerprints are protected in burns
- Permanent impairment of fingerprint pattern occurs in – leprosy, electric injury, radiation injury
- Other causes of impairment –
Atrophy of ridge: In celiac disease
Alteration of ridge: In eczema, acanthosis nigricans, scleroderma, dry skin.

Remember

- *Fingerprints can be studied by electron autoradiography, scanning electron microscopy.*
- *Lip prints are k/as cheiloscopy.*
- *DNA fingerprinting is best to detect paternity (other methods are HLA & blood group).*
- *Blackening & tattooing of skin / clothing can be best demonstrated by infrared photography.*
- *Quetelet's Rule : No two fingerprints are alike, NOT even in twins*

- **Anthropometry** : Bertillon System [after 21 yr skeletal dimensions remain unchanged]
- **Finger printing** : Galton System [Dactylography]
- **Gustafson's method** : Used for dental changes over 21 yr.
- **Poroscopy** : **Locard** method (examination of pores on fingers)
- **Podogram** : Study of footprints
- **Superimposition** : Identification by matching photographs with skull

- Chelioscopy : Identification by lip print
- Thanatology : Deals with death in all aspects
- Trichology : is the study of hairs
- Traumatology : is the study of trauma victims
- Spectrogram : Helpful in trapping anonymous phone callers
- Palatoprints : Study of laterally extended curved ridges (rugae) & grooves on the anterior part of palate.

Cephalic Index

Cephalic index is a method of identification of race.

- Skull of Indians (Aryans), Aborigines & Negros (blacks) is dolichocephalic—C.I. is 70-75
- Skull of Europeans is Mesaticephalic—C.I. is 75-80
- Skull of Mangols is Brachicephalic—C.I. is 80-85 (Palate is rounded/ horse shoe shaped, orbits and nasal opening are rounded in mangols)

- Ischiopubic index is used for sex determination
- Medullary index is used for sex from long bones (tibia, humerus, ulna, radius)
- Corporo-basal index, Alar index, and Sacral index are helpful in determining — Sex
- Cephalic index is used for identification of race.
- Ponderal's index is for IUGR ($PI = \text{fetal wt./FL}^3$)

Rule of Hasse

Rough method of calculating the age of the foetus corresponding to fetal length.

First 5 months age = $\sqrt{\text{length}}$, Last 5 months age = $\text{length}/5$

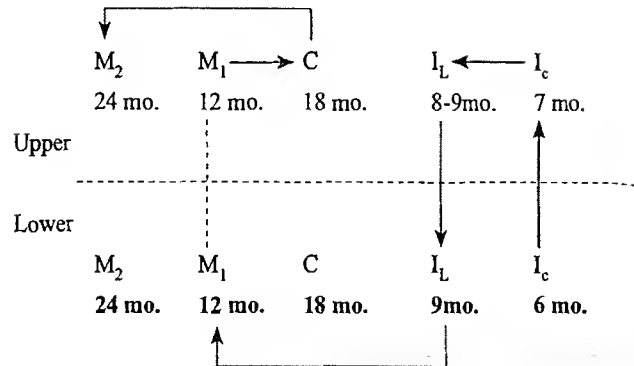
Locard's principle of exchange

When two objects come into contact with each other there is always some transfer of material from one to another.

[Remember: Poroscopy is Locard's method]

DENTITION

Eruption of temporary (primary) teeth



- In both deciduous & permanent teeth dentition occurs earlier in lower jaw (I_L is exception) & on left side
- Tooth eruption may be earlier in girls by 1 yr.
- Average temporary teeths: 6 teeth at 1 yr., 12 teeth at 1 1/2 yr., 16 teeth at 2 yr & 20 teeth at 2 1/2 yr.

Temporary Teeth (Deciduous / milk teeth)

They are 20 in number.

Dental formula is 2102/ 2102 = ICPmM/ ICPmM .

Permanent Teeth

Are 32 in numbers. Dental formula is 2123/ 2123

1st permanent teeth to erupt are lower first molars, erupt around 6-7 yr. of age (calcification of which begins at birth & completed by 9-10 years of age)

Age of eruption

Ic	IL	C	P _{M1}	P _{M2}	M ₁	M ₂	M ₃
7	8	11	9	10	6	12-14	17-25

[Mnemonic : Mama In Pain Papa Can Make Medicine :

Molar₁ (6-7 yr), Incisors central (7-8 yr), Premolar₁ (8-9), Premolar₂ (9-10), Canine (10-11), Molar₂ (12-13), Molar 3 (17-25)]

- 1st deciduous teeth/ temporary teeth to erupt is— lower central incisor left
- 1st permanent tooth to erupt— lower 1st molar [6yr.]
- Oro-dental fistula are common after extraction of — 1st Molar
- M/c tooth to be impacted is — lower 3rd molar
- Hutchinson's teeth are — Upper incisors (seen in syphilis)
- Mulberry molar / moon's molar are — Molar teeth seen in syphilis
- Dermoid teeth is — Molar
- Transparency of root of teeth is the most reliable criteria for dental age estimation by Gustafson's method.

No of teeth at different age

Age	Temporary	Permanent	Total
6 yr	18	6	24
7 yr.	14	10	24
8 yr.	12	12	24
9 yr.	12	12	24
10 yr.	8	16	24
11 yr.	4-8	20	24
12-14 yr.	0	28	28
17-25 yr.	0	32	32 (if wisdom + nt)

→ Period of mixed dentition is b/w 6-11 years

Applied Importance of Teeth

Premature dentition	Syphilis [Hutchinson's teeth] Histiocytosis-X
Delayed dentition	Cretinism [M/c cause] Rickets GH deficiency
Large teeth	IDM [Infant of diabetic mother] Hypothyroidism Large baby

- *Gustafson's method* is used for **age** estimation of adults over 21 years depending on changes in **dental tissues**. Based on 6 criteria --- Root transparency (reliable), root resorption, cement opposition, attrition, paradentosis, secondary dentine formation.
- *Stack's formula* is applied for age estimation of infants and children from height and weight of teeth. It c/b used for both deciduous & permanent teeth.
- Other formulae which c/b applied for estimation of age by secondary changes in teeth --- Point's, Mile's, Dalitz's, Boyde's

Skeletal age determination by X-ray

Age	Preferred Radiograph/X-ray	Remark
Newborn	Foot +knee	
3-9 mo	Shoulder	
1-13 yr	Hands + wrist	No. of carpal bones helpful
13-16 yr	Elbow	
17-19 yr	Ankle, femur, knee wrist	
21	Inner end clavicle + hip	Anthropometry also
20-50	skull changes	

- The age of a 15 year old female is best determined by radiographs of upper end of radius and ulna (elbow)
- For age determination of a 21 yr old female, X-ray films should be taken of --- clavicle and iliac crest
- Skeletal age is more advanced in girls compared to boys (by 1yr in early childhood & 2 yrs in mid childhood)
- Ossification centre for lower end of femur is apparent if fetus is 37 week of age It indicates maturity of fetus.
- Accuracy of sex determination is 100% by entire skeleton, 98% by pelvis + skull, 95% by pelvis alone

Difference b/n male and female pelvis

- Female pelvis is characterized by --- Obtuse suprapubic angle, larger, wider & shallower greater sciatic notch, presence of *preauricular sulcus*, small & triangular obturator foramen, and ischial tuberosity is everted

AUTOPSY & PRESERVATIVES

Autopsy procedure

- An autopsy is post mortem examination in reference to human deaths.
- A *Necropsy* is internal examination after any animal death.
- *Clinical/pathological autopsy*: Study of disease by the examination of the body after death by a pathologist. Performed to diagnose a particular d/s or for research purposes.
- During autopsy spinal cord is approached from behind (posteriorly), from occipital protuberance to lower end of sacrum.
- Acc/to Bystander post mortem procedures first to be opened is rib cage on the chest by 'Y' incision and last to be opened is -- all major blood vessels.
- Blood level of a drug is best assessed in brain.

Preservatives used in blood samples in certain suspected poisonings

- Na F ----in suspected alcohol poisoning (added to these specimens ---- CSF, vitreous, urine)
- NaCl saturated solⁿ ----Carbolic acid/phenol (NaCl is NOT used for corrosives)
- Rectified Spirit ----Cyanides, Al-phosphide, insecticides, For poisons which are not soluble in alcohol

Other specimens and preservatives

- Blood for grouping --- Blood + 25% formalin + % wt. by volume Na-citrate
- Visceras --- 10% Formalin
- Tissue for suspected Virus --- 50% Glycerine
- CSF --- Na F

Organs/body fluids preserved in autopsy

Organ preserved	Poisoning with
Brain	CO, CN ⁻ , OP, Opiates, Barbiturates, Alkaloids, Strychnine
Spinal cord	Strychnine (Nux vomica)
Heart	Strychnine, digitalis
Lung	Gaseous poisons, Alcohol, Chloroform, HCN
Bone & Hair	Heavy metals (As, Sb, Ra, Th)
Fat	Insecticide, pesticides
CSF	Alcohol
Uterus	Criminal abortion
Vitreous humour	Alcohol, chloroform
Skin	Inj. insulin, morphine, heroin, cocaine
Bile	Glutathione, cocaine, Barbiturates, methadone, narcotics

- For preservation of bone 10 cm shaft of femur is taken & for preservation of hairs 5 gm or 20-30 in numbers are taken. Nails are taken from all fingers & toes.
- During autopsy best samples for DNA extraction are taken from bone and teeth > spleen.

- Rectified spirit is NOT used as a preservative in poisoning with substances which are soluble in alcohol i.e. Phenol, Acetic acid, Phosphorus, Paraldehyde, Alcohol, Formaldehyde, Ether Chloroform, Chloral hydrate, Kerosene. [Mnemonic : PAPP- FECC]
- Sodium Fluoride (NaF) is NOT used as a preservative in poisoning with Fluorides
- Saturated NaCl is NOT used as a preservative in poisoning from corrosive acids except phenol, alkali, corrosive sublimate.
- CSF should be preserved (using NaF) in suspected alcohol poisoning
- Potassium oxalate is NOT used as a preservative in poisoning with Oxalic acid, & ethylene glycol
- Preservatives are NOT required for preserving bone, hair, nails, lungs & If analysis has to be done within 24 hours.
- Post mortem ↑ in K⁺ in vitreous helps in estimation of time since death.

WOUNDS AND INJURIES

Incised wounds

- It is clean cut through tissues caused by sharp edged weapon which is longer than its depth.
- Blood vessels are clearly cut across. So bleeding is profuse, blood escapes freely.
- Tailing signifies direction of wound.
- Heals by primary intention.

Stab wounds

- Caused by pointed weapon.
- Depth of wound > length and width.

Incised like wounds

(Incised lacerated wound)

Lacerations produced without excessive skin crushing. Caused by blunt force **over bony prominences** e.g. scalp, eyebrow, cheek bones, lower jaw, iliac crest, perineum, shin
[A / E :- chest]

Pedestrian Injuries

- Primary injuries --- D/to vehicle striking the victim.
- Secondary injuries --- D/to fall of victim on the striking object e.g. ground or other stationary object
- Primary impact injuries --- Patterned abrasions produced by object causing it. The 1st part struck (If a person is struck from behind the **back of legs** are first struck)
- Secondary impact injuries --- D/to subsequent impact (usually graze abrasions of roads) during transfer of victim in vehicle.

→ If we find extensive graze abrasions over the body of a pedestrian on road side, it could be a case of --- secondary impact injuries

→ Flaying is seen in avulsion laceration.

→ A lathi wound is an example of patterned bruise

Abrasions

Confined to epidermis only (cf contusions, which involve dermis only). Types:

- Graze abrasions
D/to the dragging of body by horizontal force. M/c type of abrasions. Also k/as **Travel rash / brush burn** (sliding / scraping / grinding abrasions)
Brush burn abrasion
Forceful contact b/n the body and a blunt object. falling

from a high ... over a stationary rough surface, A good example are grazes or brush burn abrasions seen in falls while running, 'carpet burns'

	Type	Cause	Example
Scratch		Horizontal force	Pin injury
Abrasion	Pressure	Vertical force	Ligature mark
	Imprint/ impact/ contact	High vertical force for seconds	Patterned/ pressure abrasion in Lathi wound
	Graze/ brush burn	Forceful contact b/w body & horizontal force	Fall while running, carpet burns

→ Abrasions can be mistaken for --- Ant bite

→ A lathi wound is an example of patterned bruise

Bruise (Contusion)

• Age of abrasions

Fresh	Bright red
12-24 hrs	Scab, red
2-3 d	Scab turns reddish brown
4-7d	Heals from periphery
10 days	Healing complete

Bruise (Contusion)

- A bruise is an effusion of blood into the tissues, d/to rupture of blood vessels, caused by blunt trauma
- Slight degree of violence can produce a larger bruise if tissue is vascular and loose .e.g. over face, vulva, scrotum etc.
- In ante mortem contusion, there is swelling, damage to epithelium, extravasation, coagulation and infiltration of tissues with blood, margins and edges are ill-defined. These signs are absent in postmortem bruises.
- Colour change in bruise

Time	Colour change	Due to
3d	blue	[deoxygenated Hb]
4d	blue black	[hemosiderin]
5 - 6d	greenish	[hematoidin]
7 - 12d	yellow	[bilirubin]
2 wks	normal	

- Artificial bruises c/b produced by --- Juice of marking nut, calotropis, plumbago rosea.

Grievous injury or Grievous hurt (Sec 320 IPC)

Any of the following injuries are grievous.

- Emasculation
- Permanent privation of sight of either eye/ hearing of ear.
- Privation of any member or joint
- Destruction or permanent impairing of the power of any member or joint.
- Permanent disfiguration of the head or face.
- Fracture or dislocation of a bone or tooth.
- Any hurt which endangers life, or which causes the victim to be in severe bodily pain, or unable to follow his ordinary pursuits for a period of twenty days.

→ Vitriolage (throwing of acid over face) is a type of grievous hurt.

Features of self inflicted injury

- Clothes are cut in incompatible way with number, length, and direction of wounds.
- Characteristic multiple & superficial injuries --- multiples scars of different ages.
- Chop wounds are caused by sharp cutting edge, with heavy weapon.

→ Hesitation marks / tentative cuts / trial wounds are seen in --- suicidal wounds

→ Incised wounds/ cuts on nose, ears and genitalia are usually --- homicidal

→ Fabricated wounds are mostly ---incised wounds

Antemortem V/s Postmortem wounds

- Antemortem wound is firmly adherent, there is gaping of edges of wound. Wound serotonin & histamine content is high. Vital reaction +nt
- Soft friable yellow chicken fat clot or current jelly red appearance is found in postmortem wounds. Staining can be washed away.

FRACTURE/ INJURIES OF SKULL

- Diastatic (sutural) # occur in skull.
- M/c site of skull # is temporal bone of which 80% are longitudinal while 20% are transverse #
- Fissured #
Linear # involving whole thickness of bone or inner / outer table only is the m/c type of skull #. Caused by blow with weapon having broad surface.
- Depressed #
Also k/as *fracture a la signature* [signature #] . Pattern often resembles type of weapon used. Localized depressed # are caused by blow from heavy weapon over small striking surface
- Pond or Indented # (Ping pong ball #)
Occurs in skulls of **infants /children**. Inner table is not fractured but fissured. # may occur in outer table around the periphery of dent. It also results from *obstetric forceps blade*.
- Gutter #
Part of bone is removed. Seen in tangential bullet injury wounds / firearms
- Diastatic or Sutural #
Seen in young persons d/to blow on head with blunt weapon. Sutural separation may occur
- Counter Coup #
Fracture of the skull occurring **opposite** to the site of force.
- Undertaker's #
around cervical spine d/to forcible backward falling of head after death. Tears open on the disc spaces usually around C₆₋₇₋₈
- Ring #
Fracture around foramen magnum. The so called '**motorcyclist #**' is an example of ring #. Base of the skull is divided into anterior and posterior halves each moving independently over other like a hinge

- Ring or foramen # is fissured # which encircles the skull.
- Communitied or spider web # is d/to multiple # of skull.
- In Diastatic # there is separation of sutures of skull.
- Coup means injury is located at the site of impact, and results directly by impacting force.
- Contrecoup mean lesion is present in an area opposite to the site of impact. (brain is commonly involved)
- Intermediary coup – contusion found in deeper structures of the brain along the line of impact.
- Lucid interval is a feature of EDH (extra dural hemorrhage) and insanity. During this period a person can make a valid will, can give a consent i.e. he is legally responsible for his deed.
- Heat hematoma (Burn hematoma) is seen b/w skull & duramater in thermal deaths.
- M/c type of hemorrhage in boxers—subdural hemorrhage.

Dementia pugilistica

- Seen in boxers.
- Also k/as punch drunk syndrome.
- D/to repeated minor trauma, tremors & drunken gait is seen.
- Scars and patches of gliosis are seen throughout brain

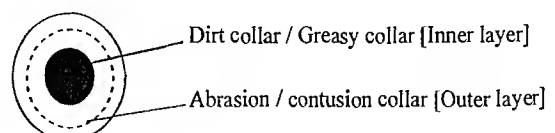
FIRE ARM INJURIES

Entry and exit wound

	Outer Table	Inner Table
Fire-arm entry wound	Punched in lesion/ clean cut hole	Bevelling
Fire-arm exit wound	Bevelling	Punched out lesion

Firearm Entry Wound

Abrasion collar (Collar burn) is seen in bullet (gun shot) injury. in entry wound from rifled bullet and it surrounds the dirt collar.



Wounds from shotgun

Wound from shotgun depends upon *distance* from which weapon is discharged

- Smoke effect [blackening] is seen upto 1 feet (30 cm)
- Flame / burning / scorching upto 1.5 feet (45 cm)
- Powder residue effect upto [unburnt & partially burnt powder/ tattooing effect] 2-3 feet (60 to 90 cm).

Entry wounds from firearms

(Revolvers and automatic pistols)

Contact shot

- *There may be no burning, no soot, no tattooing around entrance wound*
- It produces split wound, **stellate** / cruciate shaped lacerated wounds over bone [like skull]. But other usual contact wounds are oval.

Close range shot

- Tissue may be singed by flame, blackened by smoke & tattooed by unburnt/partially burnt-particles (**smudging/ fouling/blackening effect seen**)
- Entry wound in a close shot is classically **circular** and inverted but it may be irregular if gases build up
- Tattooing is seen around entry wound from a revolver or pistol, if the weapon is discharged upto 90 cm

Distant shot

- Clubbed hairs. Unburnt powder **embedded** into skin producing **tattooing** [stippling / piperling]
- No burning or soot deposition.

1 - 1.5 m - Rat hole more clear

> 2 m - Satellite pellet holes + rat hole

> 4 m - Only pellet holes⁺

Bullets

- **Tracer bullet** : Leaves a visible mark (d/to pyrotechnic display) in its flight path so that shooter can aim at target easily.
- **Tandem bullet** : Two bullets fired one after other. First bullet is ejected out of barrel by force of second bullet
- **Richochet bullet**: Bullet, which before striking aims at some intervening object first, rebounds and then hits the object

Composition of Gun powder

Black Gun Powder	75% KNO ₃ 15% Charcoal 10% Sulphur Fg, FFG, FFFg are used
Smokeless powder	1. Nitrocellulose or gun cotton [single base] 2. Nitrocellulose + Nitroglycerine [Double base]
Semi-smokeless powder	1. 85% Black powder 2. 15% smokeless powder

SEXUAL PERVERSIONS

Sadism

- Sexual gratification is obtained by physical cruelty or **infliction of pain** upon one's partner in extreme cases of sadism lust murder may be found.
- **Lust murder** is an extreme form of **sadism** in which murder serves as a stimulus for the sexual act and becomes the equivalent of coitus, the act being accompanied by erection, ejaculation and orgasm.
- Allognathia is a term synonymous with sadism.

Masochism

Sexual gratification is obtained by **suffering of pain** (M>F). Usually male gets pleasure from being beaten. Self stimulating sexual asphyxia is seen.

Fetichism

Use of abnormal objects for sexual gratification. Seen in males who use females panties, brassieres, petticoat, etc

Transvestism or Monism

Desire to be identified with the opposite sex. Person wears clothes of opp.sex. Many cases are a/w sadomasochism.

Exhibitionism

Willful exposure of genitalia in public places. Most of them suffer from compulsion neurosis or psychopath.

Voyeurism (Scotophilia)

Sexual gratification is obtained by looking/peeping/seeing sexual organs, sex act of opposite sex (peeping tom).

Occur in cases of sociopathic personality disorder.

Frotteurism:

Contact rubbing with another person in crowd.

- *Felatio* is oral stimulation of penis by male/female.

SEXUAL OFFENSES

Examination of a Rape case

- True virgin and false virgin.

Finding	True virgin	False virgin
Hymen	Intact	Intact d/to thick & elastic hymen
Fossa navicularis, Fourchette	+	Disappear
Sexual intercourse	Has not experienced	Experienced

- Hymenal rupture/tear**
 - 6 'o' clock position is the m/c site.
 - Congenital rupture - Anterior
 - Rupture d/to intercourse, trauma, FB - Postero-lateral / posterior b/w 5-7 'o' clock position.
 - Rupture d/to masturbation - 11-1 'o' clock position.
- In children hymen may remain intact after coitus as it is situated higher up (deeply situated).
- Rod used during examination : Gaba rod, Glateir Keene rod.
- Age for consent of sexual intercourse in an unmarried girl is 16 yrs.
If <16 yr, having voluntary intercourse : Statutory rape
- Age for consent of sexual intercourse in a married woman is 15 yrs.
If <15 yr, married, having intercourse : Marital rape
If >15 yr, married, forcible intercourse : NOT rape

Examination of a Sodomy case

- In case of habitual practice of sodomy changes observed in active agent are:
 - Elongation and constriction of the penile shaft,
 - Twisting of urethra
- Changes observed in passive agent (victim) are:*
 - Smooth appearance of anal skin.

- Conclusive evidence of sodomy is sperms in the anus
- Fecundation abextra**: Sperms demonstrated outside but travel inside FGT leading to pregnancy.
- Impotency** : Inability to perform sexual intercourse. E.g. in

injury at L4, L5. In these cases AIH (artificial insemination of homologous/husband) is done.

- Sterility** : Inability to beget children E.g. in vasectomized pt azzospermia is seen. In these cases AID (artificial insemination of donor) is done.
- Oligozoospermia** :
 - < 60 million /cc of sperm count.

INFANTICIDE

Hydrostatic test

It is based on the fact that on breathing, volume of lung increases & specific gravity decreases.

If lung floats in water, indicates lung of live born neonate

- Test is of no value if the liver floats
- Hydrostatic test is not necessary when**
 - Fetus is born before 180 days of gestation
 - The fetus is a monster (nonviable/deformed fetus)
 - The fetus is macerated/ mummified
 - The umbilical cord has separated and a scar has formed (cicatrization)
 - The stomach contains milk.
- Robert's sign** : is gas bubbles in LA of heart & in vessels in IUD.

→ In a live born baby hydrostatic test may become **negative** d/to--inhulation of liquor amnii, atelectasis, acute pulmonary edema, pneumonia, congenital syphilis etc.

→ **Vagitus uterinus** is a cry of unborn baby from uterus

→ **Vagitus vaginalis** is cry of an infant with head still in vagina

→ **Weight of virgin uterus** is 50 gm.

Wredin's test

It denotes changes in the middle ear in a **liveborn** neonate. Before birth, the middle ear contains gelatinous embryonic connective tissue. With respiration, the sphincter at the pharyngeal end of eustachian tube relaxes and air starts replacing this gelatinous substance. It is not a reliable test.

- Atavism** : Child resembles grandparents.
- Super-fecundation** : Fertilization of 2 separate ova, which have been discharged from ovary at the same period of ovulation by 2 separate acts of coitus.

- **Super-foetation** : Fertilization of 2 separate ova, which have been discharged from ovary at different period of ovulation by 2 separate act of coitus.
- **Suppositious** : A woman may pretend pregnancy as well as delivery and later produce a child, as if it is her own.

Battered baby/ Caffey's Syndrome

- Is also k/as non-accidental injury of childhood /child abuse syndrome and maltreatment syndrome in children.
- Bruises of different ages and SDH is common. & The typical form of this condition is very rare in India.
- Repetitive physical injuries as a result of non-accidental violence, produced by a parent or guardian, repetition of injuries at different dates, often progressing from minor to more severe.
- If the child is shaken vigorously by parents it can lead to b/l arm bruises, sub-dural hematoma, and intra-ocular bleeding.

MEDICAL ETHICS/RULES

- **Hippocratic Oath** is restated & known as Declaration of Geneva. It is followed by Medical Council of India as code of Ethics.
- **Medical Etiquette** : Deals with normal laws of courtesy followed between members of medical profession.
- Medical Ethics deals with moral principles which should be followed by all professional in their dealing with each other, potential & the state.
- Indian medical council act was passed on 1956 . Schedule 1 for India. Medical education granted by Indian universities comes under schedule 1 of MCI act. Second schedule deals with medical qualification outside India.
- Prenatal diagnosis act and Transplantation of human organs act were passed in 1994
- Declaration of Tokyo prohibits participation of a RMP in torture
- Declaration of Geneva deals with modern version of Hippocratic oath

- Declaration of Helsinki deals with human experimentation.

Starvation

- If food and water both withdrawn → 10 days survival
- If only food is withdrawn → Survival upto 60 days
- If wt loss >40% → Results in death.
- Findings:
 - Distended GB,
 - Loss of perinephric, omental & periorbital fat. Loss of perinephric fat distinguishes it from other cachexic conditions.
- M/s are darker d/to +nce of lipochrome.

THERMAL DEATHS

BURNS

- More than half of deaths from burns occur within the first 48 hrs usually from secondary shock, d/to fluid loss from burn surface.
- **Pugilistic attitude** (boxing/fencing/defense attitude) is seen in both antemortem and postmortem burns. Stiffening in this attitude is d/to coagulation of muscle proteins & dehydration which cause contraction.
- Presence of carbon particles in the terminal bronchioles on histological examination is absolute proof of life during the fire (Ante-mortem burn).
- Blood is preserved in fluoride (NaF) for analysis of cyanide in burn cases.
- **Ante-mortem burns** are char/by presence of red line, blister containing *serous fluid with albumin & chlorides*, base is red and inflamed, presence of vital reaction & enzymes, low CoHb in blood, soot in URT (*These features are absent in postmortem burn blisters*)
- **Heat hematoma** occurs when the head has been exposed to intense heat and it resembles EDH i.e. lies b/w skull and duramater.
- **Heat rupture** are multiple split wounds seen in burn deaths. usually involve extensor surfaces of joints. Heat rupture d/ to high temperature are called irregular rupture.
- *Marshall's triad* is seen in explosive bomb blast injuries.

Age of Burns

Immediately	Redness Appear
1hr.	Vesication
12-24 hrs	Exudation begins to dry
36-72 hrs	Red inflamed zone disappear, pus formed
48-72 hrs	Exudates form dry, brown crust under slough
4-6 d	Superficial, slough falls off
2-4 wk	Deep, slough falls off

Electrocution

- Joule burn (electric mark) is seen in electrical injuries (electrocution) found at the entry point of current.
- Crocodile flash burns are seen in death d/to electrocution.
- Cause of death in electrocution is ventricular fibrillaⁿ or cardiac arrest without fibrillation.
- **Zenker's degeneration** of muscles, zig-zag microfractures are seen

Lightening

- **Arborescent or Filigree burns** are seen in death d/to lightening. (branching of tree pattern or Lichtenburg's flower pattern) seen mostly over chest.

Blast injuries

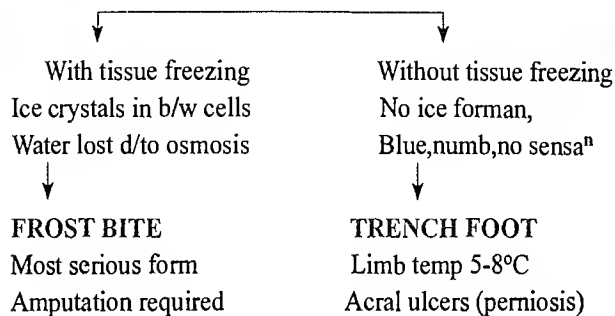
- **Airblast injuries** are m/c type in which lungs are injured.
- **Under water blast injuries** involves intestines.

→ *Air filled tissues suffer most in the blast caused by explosions*
 --- E.g. Lungs, ear, GIT

- **Hyperthermia** is defined as a temperature $>37.5-38.3^{\circ}\text{C}$ ($100-101^{\circ}\text{F}$)
- **Heatstroke**: Fever (temperature $> 104^{\circ}\text{F}$); Irrational behavior; extreme confusion; Dry, hot, and red skin; Rapid, shallow breathing. *Heat hyperpyrexia* is collapse caused by exposure to excessive heat.

HYPOTHERMIC INJURIES

- Normal body temperature is 37°C (rectal).
- Hypothermia is $< 35^{\circ}\text{C}$
- Shivering stops at 32°C .
- Body becomes poikilothermic (unstable temperature) at 30°C .
- Death occurs at the body temperature of $\leq 26^{\circ}\text{C}$.
- Hypothermic injury is of 2 types:-



POSTMORTEM CHANGES

	Favoured by / Early sets in	Delayed by	Cause
Rigor mortis	Strychnine Struggle, convulsions, Cancer, cholera TB, Typhoid, septicemia,	Death d/to Arsenic poisoning , Apoplexy death preceded by h'age, Asphyxia	Depletion of ATP
Putrefaction	Septicemia, peritonitis ↑ temp Asphyxia Moisture	Strychnine Carbolic acid/ phenol ZnCl_2 Chronic heavy metal / As	Autolysis by bacterial enzymes
Mummificaⁿ	Dry sandy soil, ↑ temp Rapid evapora ⁿ , wind As, Sb poisoning	Moisture	Dessication
Adipocere / saponification	Damp, warm, watery environment Moisture		Hydrolysis of unsaturated fats by lipases & lecithinases

- Rigor mortis sets in 1-2 hour in India.
- Adipocere formation starts in summer in 3 weeks
- In northern India post mortem staining is seen 6 hours after deaths.
- Colliquative liquefaction is seen within 5-7 days.
- Maggots appeared after 48 hours of death, help in finding time since death
- In death d/to arsenic poisoning cadaveric rigidity lasts longer than usual.

Rigor Mortis

- It is a state of stiffening of muscles, sometimes with slight shortening of the fibres.
- Depletion of ATP (d/to lack of resynthesis) to a critical level (max^m at 15%) → overlapping portions of A & M form rigid link of actomyosin → hardness and rigidity. Simultaneously, lactic acid ↑es → leads to irreversible state of contraction k/as rigor mortis
- Order of appearance
Involuntary m/s (myocardium of LV) is involved first/ within a hour of death → upper eyelids → neck → lower jaw → muscle of face → muscle of chest and UL → abdomen → LL muscle
 Disappears in same order
- Cutis anserine or 'goose skin' is d/to rigor mortis of erector pilae muscle
- It begins 1-2 hours after death, takes further 1-2 hours to develop and lasts 18-36 hours in summer & 24-48 hours in winter.
- RM is early if temperature is high or ↑ed m/s activity.
- In cold environment ATP ↓es slowly, so RM is slow.
- RM is late in adult, muscular, nutritiuos person (d/to more ATP's) while early in frail, fragile, weak & old person (d/to less ATP's)

Cadaveric rigidity

- Also k/as cadaveric spasm (cataleptic rigidity)
- Muscle that were contracted during life becomes stiff and rigid immediately after death without passing into primary stage of relaxation
- Seen after sudden death, excitement, fear, severe pain, exhaustion, cerebral haemorrhage, injury to nervous system, strychnine poisoning
- Limited to single gp of muscle usually hands
- Indicates mode of death-suicide (weapon in hand) homicide (button of assailant) or a accident (grass weeds in hand in drowning).

Post Mortem Caloricity

- Is the condition in which body temperature remains raised for the first 2 hours or so after death.
- This occurs d/to
 - Heat disturbances (CNS disorders)
 - Heat production d/to convulsions, sunstroke, tetanus, strychnine.
 - Bacterial overactivity: sepsis, cholera.
- Temperature in dead body is best measured at rectum. Rectal temp. is 1.5° F more than oral temp.
- In contrast cooling of the body (algor mortis) occurs in frostbite, barbiturate poisoning

Post Mortem Lividity (livor mortis)

- Also k/as postmortem staining/ subcutaneous hypostasis/ livor mortis/ suggillations etc.
- Caused by stoppage of circulation and stagnation of blood in vessels. Blood tends to accumulate in the capillaries and venules of dependent parts.
- Intensity of colour depends upon the amount of reduced hemoglobin in the blood.
- Fixation of postmortem staining occurs usually in 6-12 h.

Colour of postmortem lividity in certain cases.

- | | | |
|--|-----|--------------------------------|
| • CO poisoning | --- | Cherry red |
| • In Cyanide (HCN) poisoning | --- | Bright red /pink |
| • Hypothermia | --- | Bright pink |
| • Aniline | --- | Red brown |
| • In methemoglobinemia (e.g. Nitrites, aniline, KCl/ chlorate) | --- | Copper brown / Chocolate brown |
| • In phosphorus | --- | Dark brown |
| • In asphyxial death (more reduced Hb) | --- | Deep bluish violet/ purple |
| • In gas gangrene | --- | Bronze colour |
| • In hydrogen sulphide | --- | Bluish-green |
| • In Opiates | --- | Black |
| • In hypothermic body | --- | Bluish-purple/ reddish-purple |

→ Chocolate cyanosis is seen in methemoglobinemia.

→ Cherry red post mortem lividity is seen in death d/to carbon monoxide poisoning.

Putrefaction

- Decomposition of the body (**autolysis**) mainly by action of bacterial enzymes (esp anaerobic organisms from bowel).
- Putrefactive bacteria spread most easily in fluid & tends to colonize the venous system, serous cavities. D/to hemolyzed
RBCs vessel walls stain purplish-red giving marbled appearance (MARBLING).
- *First external sign* of putrefaction in a body lying in air is usually a *greenish discoloration of the skin over the region of caecum (RIF region)*. Appears in 12-24 hours.
- *First internal sign* of putrefaction is usually a *greenish discoloration on undersurface of liver*.
- Delayed in poisoning d/to carbolic acid, ZnCl, As, antimony, nux vomica (strychnine)
- Putrefaction is unlikely to develop in case of drowning in a fast flowing river.
- Colliquative liquifaction is seen within 5-7 days.
- Rate of P~ is maximum in air > water > soil/earth
- *Tache noir de lasclerotics* are early signs of putrefaction.
- *Order of putrefaction in various organs*

Larynx & trachea > Stomach, intestine > Liver > lung > brain, heart > kidney > bladder, uterus > skin muscle, tendon > bone.

- *Virgin uterus is last organ to putrefy in female & prostate in male*
- *Honey combed, vesicular or "Foamy" liver is seen.*
- *Maggots appeared after 48 hours of death help in finding time since death.*

- Earliest sign of IUD is gas in the vessel (air bubbles in heart & great arteries) → *Robert sign*.
- Emphysematous vaginitis is a/w high % of N₂ with some amt. of O₂, argon, CO₂ & H₂S.

Maceration

- Is desiccation / dehydration/ drying and shriveling of body and viscera after death.
- Aseptic autolysis seen in intrauterine deaths (late IUDs). occurs within 3-4 days, when dead infant remains surrounded with liquor but no air.
- **Spalding sign** is bec/of maceration. There is loss of alignment & overriding of skull (cranial vault) bones on X-ray d/to shrinkage of brain. Spalding sign indicates fetal death of >7 days. Spalding sign is a +ve radiological evidence of the death of a fetus in utero.

Mummification

- Is drying and shriveling of fetus d/to deficient blood supply, scanty liquor and when no air has entered the uterus.
It takes time to develop.
- Ideal conditions to develop are : High temperature, lack of moisture, free circulation of air around the body.

Adipocere

- Conversion of unsaturated liquid fats into saturated fats. Also k/as saponification
- Ideal conditions for adipocere formation are : Warm temperature + moisture, humid conditions, dead body buried in damp clay or immersed in water
- It is d/to gradual hydrolysis and hydrogenation of pre-existing fats into higher fatty acids. It has a distinct offensive or sweet smell.

MECHANICAL ASPHYXIA

Hanging

- Asphyxia which is caused by suspension of the body by a ligature, the constricting force being the body weight.
- In partial hanging, the body is partially suspended, weight of the head acts as constricting force. Hanging with the feet touching the ground indicates partial hanging
- In atypical hanging, point of suspension is **not** occiput.
- Jugular venous compression occurs with tension in rope of 2 kg, carotids by 3.5 kg & trachea by 15 kg.
- Ligature mark is situated **above the thyroid cartilage**. It is groove in tissue, pale in color, hard parchment like b/n the larynx and chin. It encircles entire neck except for the place where the knot was located. Abrasions with hemorrhage indicates ante-mortem hanging.
- '*La facies sympathetique*' is a condition seen in hanging. If the ligature knot presses on cervical sympathetic, the eye on the same side may remain open and its pupil dilated. It indicates ante-mortem hanging.
- **Saliva dribbling at angle of mouth is a sure sign of antemortem hanging.**
- P/m staining seen in legs, feet, hands and forearms.
- Hyoid bone # occurs in persons >40 years, and involves greater horn at the junction of inner 2/3rd with outer 1/3rd.
- Intima of carotid arteries shows transverse splits.

- *Lynching is a homicidal hanging.*
- *Accidental hanging is seen in masochist ---auto-erotic hanging.*
- *Ligature mark is above the thyroid cartilage in hanging.*
- *Death in judicial hanging (execution by hanging) is d/to damage to spinal cord and medulla after # dislocation of the dens (2nd cervical vertebra)*

Strangulation

- S~ is a form of asphyxia which is caused by constriction of the neck by a ligature without suspending the body.
- Ligature mark is transverse, completely encircling the neck below the thyroid cartilage.
- **Bruising/rupture of neck muscles** is common. Face is congested & cyanosed
- # of thyroid cartilage is common (but not always +nt)
- *Common methods of homicidal strangulation*
 - **Garroting** (Victim is attacked from behind by *spanish windlass*, an iron collar around neck)
 - Strangulation by ligature (horizontal ligature mark is seen):
 - Throttling or manual strangulation: death is d/to reflex cardiac arrest.
 - **Bansdola** (using strong bamboo or stick)
 - **Mugging** (Strangulation by holding the neck of the victim in bend of elbow).
- *Burking is homicidal smothering and traumatic asphyxia*
 - *Hyoid bone # is strongly suggestive of throttling.*
Chances of hyoid bone # are max^m in throttling (manual strangulation) > strangulation > hanging
 - *Inward compression # is seen in case of hanging.*
 - *Face is pale in hanging while congested in strangulation.*
 - *Avulsion# or tug/traction # of hyoid seen d/to muscular overactivity.*
 - *Method which lead to death by suffocation are--- Gagging, choking, smothering, etc.*

- *Falanga* is a method of torture. Also k/as falaka or Bastinado. In this canes or rods are used to beat on the soles of the feet, which is very painful and debilitating.
- *Telefono* is repeated slapping of the sides of the head (over ears) by the open palms of the assailant. This may cause rupture of ear drums.
- *Dry submarino* is tying of a plastic bag over the head up to the point of suffocation
- **Cattle prod** is use of electric current to torture.

Drowning

- *Signs of antemortem drowning*
 1. **A fine, copious, persistent, white, leathery froth at mouth & nostrils** is most characteristic external sign of drowning. (Increases with compression of chest even if wiped away it reappears).
 2. **Weeds/grass, mud in tightly clenched hands** (d/to cadaveric spasm)
 3. Stomach, small intestine, and middle ear containing water (in 20%)
 4. Diatoms in brain and bone marrow
- Accidental drowning is **m/c** type. Hyperventilation before any dive, deep or shallow, flushes out carbon → leads to early death.
- *Cutis anserina or goose like skin (goose-flesh skin).*
- Washerman's hands in 24 hrs.
- **Lungs are overdistended (edematous), ballooned d/to presence of fluid & air in alveoli.**
- *Emphysema aquosum* (TNT is 80% presumptive evidence of death from drowning) is seen in antemortem drowning. Edema aquosum is seen in post mortem drowning.
- *Paltanf's hemorrhages* (subpleural h'ages in lower lobes of lung d/to rupture of alveolar walls from ↑ pressure).
- *Fresh water drowning* is more dangerous than sea/ salt water drowning. Cause of death in fresh water drowning is hypervolemia, hemodilution, hyperkalemia from hemolysis & low NaCl levels. Death may occur in 3 - 5 minutes from a combination of anoxia, arrhythmias, VT and Fibrillation. Drowning in sea/salt water results in slow death.
- **Gettler test** is used for diagnosis (25% difference in Cl⁻ of Rt & Lt heart chambers is considered significant).
- **Finding of diatoms in tissue (esp. bone marrow of femur)** is highly suggestive of antemortem drowning. Diatoms are unicellular or colonial aquatic algae with extracellular silica coat. Acid digestion technique is used to extract diatoms

Fresh water and Salt water Drowning

	Fresh Water	Sea/ salt water
1. Circulation	Hemodilution, hyponatremia Lysed RBCs	Hemoconcentration, Hypovolemia shock, Crenated RBCs
2. Electrolytes	↑ K ⁺ , ↓ NaCl, ↓ Ca ⁺⁺	↑ Mg ⁺⁺ and ↑ NaCl ↑ Ca ⁺⁺
3. Cause of death	VF	Asystole or cardiac standstill (Mg ⁺⁺)

Causes of death in Drowning

1. In typical/wet/primary drowning -- Cardiac arrest, asystole (salt water)
Ventricular fibrillation (fresh water)
2. In dry drowning -- d/ to reflex laryngospasm
3. **Secondary drowning** -- Hypoxia, ARDS, sepsis, MODS, (Near drowning/ post cerebral & pulmonary edema, immersion synd.) arrhythmias etc.
4. Immersion syndrome -- Arrest d/to vagal inhibition (Hydrocution)

→ Frothing is also seen in death d/to cocaine, organophosphorus, opioids & barbiturate poisoning

Cafe Coronary Syndrome

- Death of men in restaurants and cafes who sat back in their chairs dead while eating food.
- It mimics coronary attack
- Death is usually d/to asphyxia. Reflex cardiac arrest occurs d/to laryngeal nerve stimulation

Suspended animation

- Is a condition in which vital functions of the body are at minimum (apparent death).
- Seen in electrocution, apparent drowning, heat stroke, opiate overdose, anesthetized person, deep shock/coma, yogis, cerebral concussion etc.

Hydrocution

- Also k/as *submersion inhibition* or *immersion syndrome*
- Death results from cardiac arrest d/to vagal inhibition as a result of cold water stimulating the nerve endings of the surface of the body; cold water entering ear drums, nasal passage, and pharynx/ larynx

Remember

- **Post immersion syndrome or near drowning** is a form of secondary drowning and refers to a submersion victim who is resuscitated and survives for 24 hours.
- **Scalds** is an injury which results from immersion in a liquid above 60°C or from steam (immersion in boiling water)
- **Electrocution** is an injury d/to electric current.

EXAMINATION OF BLOOD STAIN

Detection of blood in stains

- **Microscopy & chemical examination**
 - Teichmann's haemin crystal test
(-ve in old / heated / treated blood)
 - Takayama's hemochromogen crystal test -
(good result with fresh + Old stains)
- **Chemical tests**
Based on H_2O_2 & enzyme peroxidase
 - Leucomalachite green test
 - **Guaic** test
 - **Benzidine test** (especially for old blood stains)
 - Ortho toluidine test
 - Phenolphthalein (Kastle Mayer) test : Peroxidase based
- **Spectroscopic tests**
IR photography (Spectroscopy) is most delicate and reliable test for old blood stains. It detects both old & fresh stains even if the blood is in minute quantity (< 0.1mg blood)

Detection of species of blood :

Used to detect whether the blood is of human or it is of animal origin.

- **Serological test**
 - **PRECIPITIN TEST** (+ve in fresh human blood)
 - Latex test
 - Hemagglutination inhibition test
- **Enzymological test**
 - LDH, MDH, peroxidase, esterase

Detection of group of blood in stain:

- **Immunological test**
 - **Absorption elution test**
 - Absorption inhibition test
 - Mixed agglutination test
- **Enzymological test**
 - Isoelectric focusing
 - Cellulose acetate membrane
 - Vertical disc, Vertical & horizontal slabs
- Blood group antigens are found in saliva & all other body fluids except CSF.

EXAMINATION OF SEMINAL STAIN

Tests for seminal stains

- **Florence** --- detects choline

- Barberio's --- detects spermine
- Ammonium molybdate
- ACP (Acid phosphatase test)
- CPK test

[Mnemonic to remember : Cauliflower at special bar (Choline for Florence, ACP test, spermin for barbeiro)]

- Conclusive evidence of sodomy is sperms in the anus
- During medical examination of accused in alleged rape cases, presence of vaginal epithelial cells on the glans can be demonstrated by clearing the part with a filter paper and exposing it with--- **Lugol's iodine**.
- UV rays are useful in -
 - Dried seminal stain (blue white fluorescence) - Best
- IR rays (infra-red rays) are useful in identifying-
 - Old > fresh blood stain
 - Gun powder on clothes
 - Blackening, soot
 - Tattooing

CONCEPT OF DEATH

- Somatic death was coined by Bichat in 17 th century .
heart ×, lung ×, brain ×
- There is a gap of 2 hrs b/w somatic & molecular death, which is k/as supravital period. This period is useful to take organs for transplantation.
- In molecular death, individual cells die. Eye do not dilate on instillation of atropine . Sperms are non-motile.
- Concept of Brain death was given in 1967. Howard criteria were used for heart transplantation.
- Concept of Brain stem death was given in 1971. Minnesota criteria is current concept.
- Rail roading seen in retina is an immediate sign of death.

→ *Retraction balls are seen in brain in diffuse axonal injuries in concussion.*

TOXICOLOGY

* Mathieu Orfila is considered to be the modern father of toxicology.

Hemodialysis is useful in poisoning of

* Poisons with low molecular wt., low volume of distribution, low PPB

- Alcohols (Ethanol, methanol, ethylene glycol isopropyl alcohol)
- As, Br, F, Li (Arsenic, Bromides, Fluorides, Lithium)
- Chloral hydrate
- ✓ Acetaminophen, Salicylates, Valproates

* Hemodialysis is not effective in

BZD's, Kerosene, Organo-phosphorus, organo-chlorine, digitalis, Cu- sulphate poisoning

* *Copper sulphate is not a dialyzable poison*

Alkalinisation of urine / Forced alkaline diuresis

Is used to enhance renal excretion of acidic drugs--- poisoning d/to salicylates(salicylic acid), barbiturates (barbituric acid) e.g. phenobarbitone & Li, chlorpropamide, Mtx.

Acid diuresis is done for elimination of alkaloid drugs. E.g. "amphetamine, quinine."

Charcoal hemoperfusion is useful in

Poisons with high PPB & large volume of distribution, lipid soluble

- Anti epileptics (Phenytoin, carbamazepine, phenobarb)
- Paracetamol, salicylates
- Chloral hydrate, glutethimide, theophylline
- Mtx

Contraindications of

Gastric lavage	Emetics
1. Corrosive poisoning like H_2SO_4 , HNO_3 (except carbolic acid)	1. Severe heart and lung diseases
2. Convulsants, Kerosene/ petroleum compounds	2. CNS stimulant
3. Advanced pregnancy	3. Comatose patient
4. Chloral hydrate, camphor (volatile poisons)	4. CNS stimulant

* Gastric lavage / stomach wash is done with precautions in --- Marked hypothermia, upper g.i. d/s, volatile poisonings, comatose and convulsant poisoning. These are relative contraindications.

- In CuSO_4 poisoning gastric lavage carried out by
--- 1% Potassium ferrocyanide
- ✓ In Mercury poisoning gastric lavage carried out by
--- Active charcoal or
5% sodium formaldehyde sulphonylate
- In Al-phosphide (rat poison) gastric lavage carried out by
--- Saline then KMNO_4
- In Iron poisoning gastric lavage carried out by
--- 1% NaHCO_3
- ✓ Activated charcoal does not remove iron.
- Activated charcoal is usually not used in c/o paracetamol poisoning if NAC to be administered orally.
- * Coma cocktail contain Dextrose + Naloxone + Vit B_1 (DNB)
It is given when patient comes in coma & we do not met any agent of poisoning.
- CuSO_4 /atropine are used as dote & antidote .

PUPILS IN POISONING

Dilated	Constricted/	Fixed, non-reactive
Alcohol	Aconite	Large & fixed
Amphetamines	Barbiturates	- Anoxia - Anti-cholinergics
Anti depressants (TCA)	BZD	
Anti histaminics	Carbamates	Small & fixed
Belladonna (atropine)	Caffeine	- Opioids - Cholinergics
Cannabis, cocaine	Opium	
Calotropis	Organophosphorus	Variable & fixed
Cyanide	Physostigmine	✓ Hypothermia
Datura	Pilocarpine	✓ Barbiturates
Ergot, andrin	Nicotine	
Oleander, strychnine	Muscarine	

- Pin point pupils are seen in --- morphine (opium) poisoning organophosphorus, pontine hemorrhage (PO_2)
- Alternate contraction and dilatation of pupils is seen in --- Aconite poisoning, morphine (opium) poisoning

Characteristic features of some poisonings

Poisoning with	Feature
o Alcohol	Mc Evan's sign, Morbid Jealousy

- o Cocaine Magnan symptoms or formication, jet black tongue (Cocaine bugs/ tactile hallucinations), Acute MI
- o Cannabis Run amok, amotivational syndrome
- o Amphetamine Paranoid hallucinatory features (Induced psychosis)
- o LSD Bad trips, flash backs
- o Phencyclidine Dissociative anaesthesia

- Chloral hydrate is a hypnotic drug which is mixed in alcohol to induce sleep. It is also k/as "knock out drops" or "dry wine"
- Phencyclidine is also k/as 'Angel dust'
- Cocaine is often administered i.v. along with opioid (morphine/ heroin) in a mixture by the abusers k/as "Speedball."
- Cocaine bugs also k/as "Magnan sign or Magnan suaty's sign."
- * Ectasy, GHB (Ganma hydroxy butyrate), and Rohypnol are used by youngs in rave parties most of which are stimulant and hallucinogens. these drugs are k/as "Rave drugs" or sometimes "date rape" drugs.
- M/c drug of habituation is-- nicotine
- M/c substance of abuse in India is-- cannabis
- Most important drug of addiction in India is-- Opium and its derivatives
- Golden hairs are seen in poisoning d/to -- Copper
- Drugs causing necrosis of PCT (and thus nephrotoxic ATN) are--- Mercury, cadmium, phenol, CCl_4
- ✓ Date rape drugs : BZD esp flunitrazepam, alcohol, GHB are found to be misused to produce short term amnesia before rape.

MERCURY
causes
PACED
CELLY
NECROSIS

SOME IMP. POISONS

Lead (Pb)

- o Anemia, abdominal colic
- * Burtonion's /lead line [A stippled blue line in gums of upper jaw d/to lead sulphide]
- Punctate Basophilia [of RBCs]
- BAL is antidote
- ✓ Constipation, colic ↑ Coproporphyrin in urine
- o ↑ Density of metaphyseal plate of growing long bone. Drop of wrist
- o Encephalopathy in children [but rare in adult]

- Facial pallor is earliest & most consistent sign
[Mnemonic: A,B,C,D,E,F]
- ✓ Lead palsy is common in adults [rare in children]
- Plumbism/saturnism
- T/t is — Calcium disodium versenate is most effective.
BAL and penicillamine are also useful.

ZINC (Zn)

- Causes metal fume fever
- Malaria like chills are seen

ARSENIC (As)

- Mee's line (transverse nail lines)
- Marsh & Reinsch's tests are positive
- Poisoning resembles cholera
- Arsenic is rapidly cleared from blood and distributed to various organs and tissues
- Rapidly absorbed from skin & GIT. Max^m amt is seen in liver > skin. Blood sample is useful only in acute poisoning. In chronic poisoning hair, nails, skin samples are preserved
- Poison mostly excreted in hair also in nails, bones
- * Measles like fading, rain drop pigmentation
- Red - velvety stomach mucosa, hyperkeratosis of palm & soles → Bowen's d/s is d/to malignant transformation of palmar keratosis.
- Antidote : freshly precipitated hydrated Fe₂O₃
- Subendothelial petechial hemorrhage of ventricles.
- Can be detected in completely decomposed bodies.
- Most popular homicidal poison

MERCURY (Hg)

- Acute mercury poisoning resembles "Diphtheric colitis". Involves ascending and transverse colon. Presentation may resemble pheochromocytoma or Kawasaki disease.
- Triad of symptoms : Excessive salivation + tremors + neuropsychiatric changes.
- Most poisonous salt of mercury is corrosive sublimate or mercuric chloride (HgCl₂). Gastric lavage with sodium formaldehyde sulfoxylate, reduces mercury chloride to metallic mercury.
- Mercurous chloride known as calomel
- Maternal intake of organic mercurial compounds during pregnancy may lead to cerebral palsy in neonate.

Chronic Hg poisoning

- ✓ Blue line at gums on junction with teeth.
- ATN (damage to PCT of renal tubules) and MGN in kidney
- Acrodynia/Pink disease
Generalized rashes & idiosyncratic reaction in children
- Minamata d/s : d/to eating of fish poisoned by methyl mercury. (Hunter Russel syndrome). Tunnel vision is seen.
- Mercuria lentis : Brownish deposits Hg on anterior lens capsules. It is B/L and has no effect on vision/ visual acuity.
- ✓ Hatter's /Glass blower's shake are fine tremors of tongue, hands, arms and later of legs (Shaking palsy). Common in workers of glass and hat industry (d/to Hg-nitrates)
- Erethism /Hydragyria — neuro-psychiatric manifestations of mercury such as anxiety, depression, shyness, timidity, irritability, loss of confidence, amnesia, & insomnia are seen in mirror manufacturers. (Mad as hatter)
- Antidote of choice for mercury poisoning — BAL.
Ca-EDTA should not be used as it ↑ nephrotoxicity

CYANIDE poisoning (Prussic acid /HCN)

- HCN is colourless, volatile liquid with odour like bitter almond
- Toxicity c/b caused by : sodium nitroprusside
- Cyanide inhibits the action of cytochrome oxidase; carbonic anhydrase and other cellular enzymes. Thus it causes cellular asphyxia by histotoxic or cytotoxic action
- CVI : loss of consciousness (fixed dilated pupils, areflexia)
- Achlorhydric patient do not suffer from cyanide poisoning as conversion into chlorides and hydrocyanic acid by HCl does not occurs
- P/m staining is pink or cherry red in color.
- * Congestion of viscera is common. Stomach mucosa is red, velvety & congested.
- T/t:
In cyanide poisoning Lilly's antidote kit is used coupled with high flow O₂ & artificial respiration
(Amyl nitrite → Sodium nitrite → Sodium thiosulfate/ methylene blue)

✓ HISTOTOXIC
 ✓ HYPOXIA
 ✓ BITTER ALMOND

→ *HCN
 → *CO
 → *phosgene

**

- Nitrites used in t/t act by converting CN^- to methemoglobin (or Hb to MetHb)
- HCN is used for suicide and cattle poison & in some countries for legal execution
- Elevated levels of cyanide in blood are seen in thermal burn deaths esp. where plastic/paints are burning
- * Poisons affecting diffusion of oxygen at cellular/tissue level (histotoxic) are--- CO, HCN, phosgene

Aluminium phosphide (CELPHOS) poisoning

- Acute Al-P (Celphos) is extremely lethal
- ✓ Al-P inhibits cytochrome C oxidase
- Produces phosphine gas on contact with moisture
- D/g : Garlicky/decaying fish odor from mouth, AgNO_3 test for confirmation.
- C/I/F : Sub-endocardial infarction, esophageal stricture, arrhythmias.
- * Gas chromatography is most sensitive and specific for detection of phosphine (PH_3)
- * To reduce the absorption gastric lavage is done by KMnO_4 .
- ✓ No specific antidote.

ALCOHOL

- Absolute alcohol contain 99.95% alcohol.
- Rectified spirit contain 90% alcohol.
- * Alcohol disappears from blood @ 10-15 ml/hr.
- Fatal dose of alcohol is 150-200 ml of absolute alcohol.
- Methods for detection of blood or urine alcohol levels are --- ADH, Cavett test, Kozelka & Hinc test, Gas chromatography "most specific"
- Mc Ewan's sign positive (in alcohol intoxication pupils are contracted but stimulation of the person by pinch/slap causes them to dilate with slow return)

- Widmark formula is used for blood or tissue alcohol conc. (Quantity of alcohol in the body) It takes into account the size, sex of the person and type of alcohol consumed.
- Gas liquid chromatography is the best method for estimation of alcohol for medicolegal purpose.
- ✓ Beer drinker's cardiomyopathy is d/to cobalt.
- ✓ Munich beer heart is d/to alcoholism.

Methyl alcohol

- Toxic effects of methyl alcohol (methanol) are largely d/to formic acid Optic atrophy c/b caused by methyl alcohol poisoning.
- T/t of methyl alcohol poisoning is ethyl alcohol.

CANNABIS

- Cannabis also K/as Indian Hemp hashish or marihuana
- Active principle is tetrahydrocannabinol (THC). It is CNS stimulant
- ✓ Run amok is a feature of chronic cannabis poisoning.
The person develops psychic disturbance marked by a period of depression, followed by violent attempts to kill people (impulse to murder) After killing the person may commits suicide.
- * Hashish Insanity: The person becomes insane and may suffer from hallucinations and delusion of persecution.
- Bhang - prepared from dry leaves and fruit shoots
- Ganja - prepared from flower top of the female plant
- Majoon - sweet from bhang (produces delusion of grandiosity)
- ✓ Charas / Hashish - resin exuding from leaves and stem of the plant cannabis sativa/ indica

BARBITURATES

- CNS depressant. Large doses directly depress medulla
- * First symptom is drowsiness. Stupor progressing to coma, loss of reflexes, gradual loss of response to painful stimuli, +ve babinski sign, respiration may be rapid, shallow (Cheyne stokes respiration)
- O/e - Hypotension, cyanosis, cold clammy skin, ↓ peristalsis, hypothermia. Pupils are usually slightly constricted and reactive but dilate in terminal stage.
- Barbiturate blisters → Blisters on the skin often on an area of erythema strongly suggests barbiturate poisoning. Commonly found in interdigital clefts, inner aspect of knee, back of calves and forearms.
- ✓ Liquid gold urine (oliguria with dark urine)
- * Death is d/to respiratory failure or VFI.
- T/t:- Gastric lavage, Scandinavian method, hemodialysis followed by forced alkaline diuresis with mannitol is TOC. Hemoperfusion through a column of activated charcoal
- ✓ Barbiturates are most commonly used as suicidal poison.
- ✓ Automatism can lead to accidental barbiturate poisoning.

DATURA

- Fruit (morphologically) look alike Ricinus communis (beans of castor seeds).
- * Datura seeds look like capsicum seeds.

ADH
Cavett test
Kozelka
Hinc test

SIZE
SEX
TYPE
of alcohol

✓ Muttering delirium are seen.

pill rolling movement, tachycardia, "carphologia" are seen.

• Intoxication is characterized by : 9 D

- Dry and hot skin (dry as bone & hot as hare)
- Dilated pupils (blind as bat)

✓ Dilated vessel, Flushed face (red as beet)

- Delirium (mad as wet hen)

* Dermatitis

- Dysphagia
- Diplopia
- Delusions

PHENOL (Carbolic acid)

✓ CNS depressant

* Brownish and leathery stomach

• Causes "smoky green urine (carboluria)" d/to compounds pyrocatechol and hydroxyquinones. Urine turns black on standing.

* Constricted pupils, cartilage/corneal discoloration seen.

H₂SO₄ (Sulfuric acid)

- Scalded gastric mucosa
- In the tongue, necrotic areas are greyish white (lips, tongue, mouth) but soon become brown/black.
- Used for vitriolage.

✓ Xanthoproteic reaction is seen d/to production of picric acid in HNO₃ poisoning.

✓ Vitriolage is caused by H₂SO₄

→ Pulmonary edema is caused by : Heroin > cocaine > DPH > Trauma

Stomach mucosal appearances in various fatal poisoning:

Color/appearance	Poisoning/condition
Pale	Snake
Congested	BZD, Al. P, OC, OP
* Hyperemic congested	Alcohol, Snake, Al.P (Aluminium phosphide), OC, OP
Fiery red	OC (Organochlorine), OP (Organophosphorus)
Scalded	H ₂ SO ₄

Organophosphorus poisoning

- Organophosphates inhibit cholinesterase at esteric site.
- 2 types:
 - Alkyls :
 - * Aryls : aryls are more poisonous. E.g. parathion, paraoxan, chlothion, diazinon (Tik-20)

- Seen in farmers presents with vomiting, diarrhoea, salivation, perspiration, miosis & pulmonary edema
- * RBC cholinesterase level is most specific.

• Asthma like symptoms are seen.

• Antidotes are Oximes, which "attach at esteric site" and act as re-activator. They are "contra-indicated in carbamates poisoning".

PHOSPHORUS poisoning

✓ Garlic like odor.

• Phosy jaw (Glass jaw) is seen - d/to white phosphorus.

* Diwali poisoning.

✓ Smoking stool syndrome.

* Antidote : CuSO₄ > Vitamin K.

ACONITE poisoning

• Causes numbness and tingling in the limb

✓ Burning sensation in the mouth and oro-digestive tract.

Intense thirst, dryness of mouth in later stages.

* Pupils alternatively contract and dilate k/as hippus

* Hypotension, arrhythmias, AV block may occur.

FATAL DOSES OF POISONS

50 mg	100	180	200	260	800 mg	1 g
Heroin	TEPP	As ₂ O ₃	Morphine	HCN	Codeine	Pethidine, diazinon, malathion, HgCl

1 g	2 g	6 g	20 g	500 mL
Pethidine, diazinon, malathion, HgCl	Raw opium	Endrin	DDT, Paracetamol	Ethyl alcohol (absolute alcohol)

Characteristic Odour in Poisoning

Cyanide	Bitter almond
* Arsenic, ZnP, Al-P (Celpos), Phosphorus	Garlic odour
H ₂ S	Rotten egg
Zn-phosphide	Fishy
Carbolic acid	Phenolic odor
Kerosene, Organophosphorus	Kerosene like
Cannabis	Burnt rope
Ethanol	Fruity

POISONING & THEIR SPECIFIC ANTIDOTES

Poisoning with	Antidote
Anticholinergic drugs (Atropine, TCA)	Physostigmine
Organophosphates →	Atropine, 2-PAM (pralidoxime)
Ethylene glycol	Fomepizole > ethanol
Methanol	Ethanol > 4MP (4methyl pyrazole) / fomepizole
Narcotics, clonidine	Naloxone
Cyanides	Dicobalt edetate, PAPP
Nitrates, nitrobenzenes	Methylene blue
Paracetamol →	N-Acetyl cysteine (NAC)
BZD (Diazepam)	Flumazenil
Ergotism →	Sodium nitroprusside
Arsenic →	Freshly Precipitated hydrated ferric oxide (Fe_2O_3)
Mercurial compounds (Corrosive sublimate etc)	Sodium formaldehyde sulfoxylate
Oxalic acid	Calcium gluconate

✓ DOC for early mushroom poisoning : Atropine (d/to muscarine excess).

→ Endrin is considered as plant penicillin.

Treatment of Overdose

Toxicity / overdose of :	Antidote
◦ Sympathomimetic / theophylline toxicity	--- β -blockers
◦ Irritant gases	--- Budesonide inhalation
◦ Insulin	--- Glucose
◦ β -blockers, CCB, Hypoglycemics	--- Glucagon
✓ Co, H_2S	--- Oxygen (HBO)
◦ Heparin	--- Protamine sulphate
◦ Digitalis	--- Fab antibodies
◦ Dicumarol toxicity	--- Vitamin K

Chelating agents in heavy metal poisoning

Chelating agent	DOC/most useful for	NOT effective for
✓ BAL (Dimercaprol) →	Mercury & Arsenic	Fe, Cd, CN
Ca- Na_2 EDTA (versenate)	Pb (Lead)	Hg
✓ D-penicillamine	Cu (also for Hg Zn, Pb)	Fe

* Triantene is a Cu-chelator (also useful in Wilson's disease)

→ EDTA & DTPA (pentetic acid) have anti-oxidant action & both are also useful in poisoning with radioactive metals.

→ Large doses of EDTA are used in carbonic anhydrase enzyme inactivation. EDTA chelates with the metal ion of enzyme.

Some imp. poisons---

Stupefying	- Datura ✓ Cannabis Indica (Bhang) - Chloral hydrate
Cattle poison	- Abrus precatorius ✓ Aconite - Arsenic - Zinc Phosphide - Organophosphorus ✓ Nitrite - Calotropis ✓ Hydrocyanic acid (<u>linseed plant</u>) [mnemonic : NAAACHO - Zi]
✓ Aphrodisiacs (love philters)	- Cocaine - Cannabis - Opium - Cantharides - Arsenic - Nux vomica
Abortifacient	- Calotropis - Oleanders - Lead - Aconite - Ergot
Colourful poisons	✓ Carbolic acid (smoky green urine) - Oxalic acid (<u>white brown</u> patches) - Copper (blue green mucosa/color of vomitus) - Arsenic (red-velvety)
Artificial bruise	✓ Semicarpus anacardium ✓ Mader juice ✓ Plumbago

Gases

✓ Sewer gas is --- H_2S , CO_2

◦ Laughing gas is --- N_2O

◦ Laughing gas is --- N_2O

pyalism ... poisoning

- Ideal homicidal poisons — fluoride (rodenticide), Arsenic (best), Aconite, Thallium
- Ideal infanticidal poison — Opium
- Ideal suicidal poisons — Organophosphorus, Endrin, Opium, Barbiturate, Oleander
- * Japanese suicidal technique — Based on detergents/mixing common household chemicals in cloud of gases
- Calabar bean is — Ordeal poison of choice flourishes in warm tropical climate of Africa.
- Cardiac poisons are — Digitalis, Nicotine, Oleander, Cyanide, Aconite, Quinine
- Asthma like symptoms are seen in — organophosphorus poisoning
- Diwali poisoning is d/to — phosphorus
- Poisoning resembling cholera — Arsenic
- * Pyalism is seen in — copper poisoning

* In head scales 3rd labial touches the eye and nasal shields (in cobra/coral snake)

* Undersurface of the mouth has only 4 infralabials. 4th being the largest in Kraits

→ Fatal dose of Krait venom is minimum (6 mg).

→ Hematuria is caused by bite of Russell's viper

* Neostigmine is beneficial in symptomatic bites by cobra.

Cantharide poisoning

Char / by vesicles blister formation, strangury and priapism

"PRIAPISM"

SNAKES

- o Cholinesterases are found in Cobra venom which ↓ ACh → M/s weakness → death within a day d/to resp. failure.
- o Unexplained b/L ptosis is the earliest sign d/to cobra venom.
- * Bleeding is d/to phosphatidases, found in viper

Poisonous Snakes

- o Elapidae family (Cobra, Krait) — Neurotoxic [CNS/Khopadi]
- o Viper — Hematotoxic, vasculotoxic (d/to phosphatidases)
- o Sea/Marine snakes — Myotoxic (marked muscle weakness, polymyositis)

On Urine Examination

- o Albuminuria is seen in — Krait's bite ✓
- o Hematuria is seen in — Viper bite ✓
- o Myoglobinuria is seen in — Sea snakes ✓

Poisonous Vs Non-poisonous snakes

	Poisonous	Non-poisonous
Head scale	Small (in viper)	<u>Large</u>
Belly scale	<u>Large</u> , covers entire breadth	<u>Small</u>
Teeth	Two long fangs	<u>Multiple small teeth</u>
Tail	Compressed	Not compressed
Habits	Nocturnal	
Examples	Viper, cobra, krait, sea snakes in India	<u>95% of Indian snakes</u>

SOME POINTS OF QUICK REVISION

- o Pugilistic attitude (boxing, fencing or defense attitude) is seen in burns
- o Sexual asphyxia is a/w — masochism
- ✓ Joule burn is seen in electrocution, found at point of entry of current
- ✓ Arborescent or Filigree burns (Lichtenberg's flowers pattern) are seen in - lightening.
- ✓ Crocodile / flash burns are seen in - electrocution.
- o Paleness of face, oblique ligature mark, Hyoid bone # and saliva drooling out of mouth is suggestive of death due to - Hanging.
- o Congested / flushed face, marked with petechiae, transverse ligature mark, # of thyroid cartilage, emphysematous bullae on surface of lungs are seen in death due to - Strangulation.
- ✓ Presence of fine, white, Lathery froth at mouth & nostrils is most suggestive of - Drowning.
- o Weeds in hands, washer man hands, emphysema aquosum, Paltauf's hemorrhages and +ve. Gettler test is seen in death due to - Drowning.
- * Naltrexone — drug that reduces craving for alcohol
- o Drug used for psychoanalysis is — Scopolamine (Levoduboisine) and hyoscine which c/b administered by transdermal patch
- o Caustic poisons corrodes mucosa bec/ of hygroscopic action.
- o Aluminium phosphide is kept in translucent bottles as a waxy liquid.
- o Sparrow foot marker seen on the face is bizarre shaped lacerations d/to contact with shattered windshield glass.

Seen in front seat passengers in RTAs.

- **Punnet square** is a diagram that is used to predict outcome of a particular cross study or breeding experiment by biologists to determine the outcome of an offspring of a particular genotype.

NEGATIVE POINTS

- NOT a tests for seminal stains ----- Luminal test, Fluorescence test
- Gastric Lavage is NOT useful in poisoning with ----- Kerosene
- NOT seen in organophosphorus Poisoning ----- Tachycardia
- Gun powder mixture does NOT contain ----- Lead
- NOT a characteristics of postmortem burn ----- +nce of enzymatic reaction, red line.
- NOT seen in ante-mortem burn ----- Air filled vesicles.
- NOT commonly seen in lead poisoning in adults ----- Encephalopathy.
- NOT seen in acute kerosene poisoning ----- ARF.
- NOT a characteristic of antemortem wounds ----- Chicken fat clot.
- NOT a constituent of black gun powder ----- Lead peroxide
- Inquest NOT conducted in India ----- Medical examiner inquest (Inquest by a doctor)
- **NOT a sign of intrauterine death -----Adipocere formation, putrefaction**
- Method which does NOT lead to death by suffocation----- Smothering
- Poisoning which does NOT affect diffusion at tissue level --- Curare (It affects conduction at N-M level)
- Preservative NOT used for corrosives --- NaCl
- NOT present in heat stroke --- sweating
- NOT a methods which leads to death by suffocation ---Throttling
- NOT a characteristic feature of antemortem contusion (bruise) ---Edges are sharply defined
- NOT an example of traumatic/ crush asphyxia --- Accidental strangulation
- Embalming fluid in India does NOT contain --- Ethanol
- NOT true of lightning flash injury --- Compression effect d/to air movement in its direct wave.
- NOT a cause of indoor air poisoning ----- Mercural gas
- NOT a tests for seminal stains ----- Luminal test,

CLINICAL VIGNETTES

- A housewife ingests a rodenticide white powder accidentally. She is brought to hospital where the examination shows generalized, flaccid paralysis and an irregular pulse. ECG shows multiple ventricular ectopics, generalized changes with ST-T. Serum potassium is 2.5 mEq/L. The most likely ingested poison is:

A. Barium carbonate. B. Superwarfarins
C. Zn-phosphide D. Al – phosphide

(Ans: D. Al – phosphide)

Cl/f of poisoning in.

$BaCO_3$

Used as rat poison. Cl/f are - GI irritation, cramps stiffness of muscles, heart may stop in systole. Most characteristic changes are areflexia and paralysis.

Zn-phosphide

Vomiting, diarrhea, cyanosis, fever, respiratory distress.

Al – phosphide

Inhibits respiratory chain enzymes (ETC) by inhibition of cytochrome oxidase. M/s weakness, paralysis, cardiac arrhythmias

- A pest control worker was brought to the emergency room with h/o acute pain abdomen and vomiting. There is garlic odour of breath, and transverse lines over nails. The most likely ingested poison is: [AIIMS May'06]

A. Lead B. Arsenic
C. Phosphene D. Mercury

(Ans: B. Arsenic)

Arsenic is a pesticide used as a paste to control rodents. Arsenic is highly toxic compound. It has characteristic garlic odour. Gastrointestinal symptoms (pain abdomen, vomiting, diarrhoea) are common in acute poisoning.

- A teacher slapped a student causing 25% hearing loss in her left ear. A surgeon operated on her and restored her hearing. The teacher is guilty of causing [AIIMS Nov'09]

A. Simple injury B. Grievous injury
C. Dangerous injury D. Serious injury

(Ans: Grievous injury)

Loss of privation of sight or hearing is considered grievous hurt. Which need not be complete but c/b partial but has to be permanent. Permanent does not mean that it is incurable.

NOTES

- A doctor is examining habitual active agent of sodomy after he confesses that he is active agent. Which of the following will not be seen? --- [AIPGMEE'12]

- A. Fecal contamination over penis
- B. Reconstruction of shaft of the penis
- C. Smegma on the glans
- D. Rupture of the frenulum

(Ans. C. Smegma on the glans)

In case of habitual practice of sodomy changes observed in active agent are:

Elongation and constriction of the penile shaft

Twisting of urethra

Changes observed in passive agent (victim) are:

Smooth appearance of anal skin.

- A child presents with unknown ingestion of substance followed by dilatation of pupils, bronchodilatation, delirium, tachycardia, hot and flushed skin, dry mouth . Most likely cause is toxicity of --- [AIIMS May'10]

- A. Anticholinergic compound
- B. Opioid
- C. Cholinergic
- D. Sympathomimetic drug

(Ans. A. Anticholinergic compound)

Child in the question is showing clinical symptoms & signs of Datura poisoning (anticholinergic compound)

Dhatura intoxication / ingestion is c/by

- Dry and hot skin (dry as bone & hot as hare)
- Dilated pupils (blind as bat)
- Dilated vessel, Flushed face (red as beet)
- Delirium (mad as wet hen)
- Dermatitis
- Dysphagia
- Diplopia
- Delusions [9 'D']

Cholinergic ingestion is c/by

Constricted pupils, bradycardia, abdominal cramps diarrhoea, salivation, bronchospasm

Sympathomimetic ingestion is c/by

Dilated pupils, tachycardia, excessive sweating (diaphoresis), hyperglycemia

Opioid ingestion is c/by

Constricted/ pin point pupils, respiratory depression, hypothermia/ cold skin.

NOTES

INFECTIOUS DISEASE EPIDEMIOLOGY

Types of prevention

	Primordial Prevention	Primary Prevention	Secondary Prevention	Tertiary Prevention
<i>Definition</i>	Prevention of emergence of risk factors in population in which they have not yet appeared	Action taken prior to the onset of disease (In pre pathogenesis phase)	Action to interrupt progress of disease & its c/c	Intervention in late pathogenesis phase
<i>Modes & examples</i>	<i>Lifestyle modification</i> (e.g. avoidance of smoking, fatty diet, exercise to avoid risk of CHD or HTN, source reduction in malaria)	<i>Health Promotion</i> <ul style="list-style-type: none"> Health education (most cost effective intervention) Lifestyle & behavioural change Nutritional intervention (food fortification) Environmental (safe water/housing). 	<i>Specific Protection</i> <ul style="list-style-type: none"> Immunization against VPDs Vit A in children. Contraception (STDs) Chemoprophylaxis Protection against occupational hazards, accidents, allergens, carcinogens. Bed nets Quarantine 	<ul style="list-style-type: none"> Early diagnosis (screening test, case finding) e.g. pap smear for Ca Cx Treatment e.g. in T.B., leprosy STD Disability limitation Rehabilitation
<i>Best applied in</i>	Chronic diseases, Coronary heart d/s, hypertension	VPDs	TB, leprosy, STDs	Poliomyelitis

- Primordial prevention is the best method of promoting healthy life-style in children and is best for non-communicable diseases (DM, CAD, HTN etc).
- Yoga can be considered under preventive medicine.
- Health education is one of the most cost effective interventions.
- Health programmes initiated by the governments are usually at the level of secondary prevention.
- Disability prevention relates to all the levels of preventions (e.g. in polio)
 - Decreasing the occurrence of impairment by immunization (1°) 3 doses of OPV in early infancy.
 - Disability limitation by T/t (2°).
 - Preventing the transition of disability into handicap (3°)
- In a diagnosed case of RF, Penicillin injections are recommended every 3 weeks, which is an example of early diagnosis and treatment (secondary prevention).

Disease control / Elimination / Eradication

Disease	Control	Elimination	Eradication
<i>Definition</i>	Operations aimed at ↓ing incidence, duration and risk of d/s, keeping the frequency of d/s within acceptable limits	Interruption of transmission of d/s. Agent is present.	Termination of all transmission of infection by extermination of infectious agent
<i>Importance</i>	Most control programmes focus on 1° and 2° prevention	Regional elimination is an important precursor of eradication	Agent is not present in natural environment
<i>Example</i>	Malaria	Leprosy, Yaws	Small pox (eradicated)

- India has eliminated 3 diseases : Dracunculiasis, Yaws, leprosy.
- World has eradicated /Globally eradicated - Small pox
- Disease under global eradication campaign are polio, measles and dracunculiasis
- India will eliminate in near future -- Leprosy, kalazar, filariasis, polio.

Mass treatment approach

(Mass chemoprophylaxis) is used in 2^o prevention, in control of certain d/s e.g. yaws, pinta, bejel, trachoma, malaria, endemic /lymphatic filariasis, plague.

Iceberg phenomena

Differentiates b/w apparent and inapparent (subclinical) infection. NOT shown by measles, rubella, rabies, tetanus.

Quarantine

- Healthy individual isolated after exposure to disease for **longest** incubation period of that disease (kept under observation) (in contrast to isolation Q~ applies to restrictions on healthy contacts of infectious disease)
- Duration : Maximum incubation period.
- First applied for plague (40 days mean). 6 days for yellow fever.
- In epidemic cases surveillance is done for double the incubation period

Surveillance

- Data collection and analysis for action.
- Passive S~ --- when data / reports are sent by designated health facilities or individual on their own, periodically as routine
- Active S~ --- S~ is active when designated official, usually external to the health facility visits periodically & seeks to collect data from individual or registers, log books, medical records at a facility to ensure that no reports / data are missing / incomplete.
- **Sentinel S~** is a method for identifying missing cases and thus it supplements notified cases.

EPIDEMIOLOGICAL METHODS

There are 3 aspects of morbidity

- Disease frequency --- Measured by incidence and prevalence rates
- Disease duration --- Measured by disability rates
- Severity --- Measured by CFR (case fatality rate)

Different observational study designs to---

	Eco-logical	Cross-sectional	Case-control	Cohort
Investigate rare d/s	++++	-	++++	-
Investigate rare cause	++	-	-	++++
Investigate long latent period	-	-	+++	-
Test multiple effects after single exposure (of a cause)	+	++	-	++++
Study multiple exposure & determinants	++	++	++++	+++
Measure time relationship	++	-	+(If prospective)	++++
Directly measure incidence	-	-	+(if population based)	++++
Cost	low	medium	medium	high
Chances of bias				
Selection bias	N/A	↑	↑↑	↓
Recall bias	N/A	↑	↑	↓
Loss to follow up	N/A	N/A	Low	High
Confounding	↑↑	↑	↑	↓
Time required	low	medium	medium	high

[+++++ Most suitable, - not suitable, N/A not applicable]

Case control / retrospective study

- Common first approach to test causal hypothesis
- Precedes from effect to cause (study of a person who had already contracted the disease)
- Multiple etiological factors of a disease can be found.
- Smoking & lung cancer relationship is determined by odds ratio
- **Merits**---Good for rare d/s, No risk to subject, inexpensive.
- **Nested case control study design** is a prospective study design.

Type of Study	Study design	Also k/as	Unit of study	Possible measurements	Suitable for	Not suitable for	Demerits
Descriptive			Population				
	Ecological (Correlational)		Group of people, Population	Incidence	Group characters	Measuring incidence	
Analytical	Cross sectional		Individual	Prevalence, proportion	Chronic d/s	Rare d/s, rare cause	
	Case control (case reference study)	Retrospective study	Individual	Odds ratio	Rare d/s, Ix of multiple exposure & its determinants		
	Cohort (Follow up)	Prospective/longitudinal study	Individual	Incidence, RR, AR, survival	Chronic d/s, Ix of rare cause, Single exposure & its effects	Rare d/s,	Costly, Long term follow up
Experimental/Interventional	Experimental		Individual	Incidence, RR, survival			
	RCT/Clinical trials		Patient				
	Field trials	Community intervention studies	Healthy people				

Cohort study

- Also k/as prospective study, longitudinal study, forward looking study or incidence study.
- Proceed from cause → effect. Reserved for testing of precisely formulated hypothesis.
- Multiple outcomes after a single exposure (etiological factor /cause) are possible.
- Merits ---Incidence is measured
- Demerits---Not suitable for rare disease, Subject is exposed to risk, Long follow-up is needed (costly)
- Valid or Good association b/n d/s and cause (e.g. smoking and lung cancer) should be there or incidence should be high for cohort study.
- A cohort study is the best way to identify incidence & natural Hx of a d/s and can be used to examine multiple outcomes after a single exposure.
- Potential bias in recall & observation is lessened since exposure can be determined prior to event.
- Relative ability of a study design to prove causation
The best evidence comes from well-designed RCTs (++++)
cohort & case control (+++) cross sectional and ecological (+).
- However, evidence comes most often from **observational** studies.
- Most accurate results are obtained from meta analysis (systemic reviews).
- Strength of causal association b/w cause & effect is measured by the size of the risk ratio (relative risk)
- Longitudinal study is for incidence and acute d/s. Used to study natural h/o d/s and to identify risk factors
- Most preferable observational or analytical study design is cohort study
(incidence of d/s is calculated by prospective /cohort study & longitudinal study)
- Bland & Altman analysis is a statistical method which is used to compare a new diagnostic method with the gold standard.

BIAS / Systematic error

It is the result of a systematic error in the design or conduct of a study.

• Memory or recall bias

When cases and controls are asked about their past Hx, it is possible that more the cases to recall the existence of certain events than controls who are healthy people. The systematic distortion of retrospective study.

• Selection bias

Occurs when the cases and controls selected are not representative of general population.

• Attention bias / Subject bias

Subject under study may alter behaviour systemically when they know they are being observed (**Howthorne effect**).

• Measurement/classification bias

Bias in collecting data.

• Berkensonian bias

Also k/as **admission rate bias**. Bias d/to difference in the rate of admission to the hospital. It is a type of selection bias (Selection followed for hospital admission).

• Confounding bias

Can be minimized by matching.

• Neyman bias

Prevalence-incidence bias. A late look at those exposed (or affected) early will miss fatal and other short episodes, plus mild or silent cases and cases in which evidence of exposure disappears with d/s onset

→ Double blinding is done to avoid subject variation and observation bias

→ Epidemiological triad includes --- agent, host and environment.

Confounding

- Factor a/w both exposure and d/s is called confounding factor

The confounding variable must be related to the d/s in question. For a variable to be confounder, it **must** be a determinant of the occurrence of d/s and with the exposure under investigation.

- The confounding variable is distributed **unequally** b/w exposed and unexposed populations
- Mantel- Haenszel procedure is used to control observations in different groups/ strata

- In the design phase the confounding variable is eliminated/ controlled by :

- **Randomization** : Is done to eliminate *unknown* confounding factor and it is done in experimental studies. Randomization is the heart of a trial. It is superior to both matching & blinding.
- **Matching** : Is done to eliminate known confounding factor . It is done in analytical studies to ensure comparability b/w cases and controls.
- **Restriction** : Restriction of the study to a sub group who have a particular characteristics

- In analytical phase (during analysis of result) the confounding variable can be controlled by :

- Stratification
- Statistical modelling (multivariate)

Association

The concurrence of two variables more often than would be expected by chance. Association does not necessarily imply a causal relationship

Correlation

Indicates the degree of association b/w two variables or characteristics. Correlation co-efficient ranges from -1 to +1

- Association is simultaneous existence of 2 variables
- Correlation is relationship b/w 2 qualitative or continuous variables
- Regression provides structure (quantification) of relationship b/w 2 quantitative variables

In chronic d/s epidemiology criteria for establishing association and causation

- Temporal association
- Strength of association
- Biological plausibility
- Coherence and consistency of association

Measures of association

- p-value
- Odds ratio (Cross product ratio): Is derived from case control study. It is a measure of the strength of association b/w risk factor and outcome
- Correlation and Regression co-efficient
- Differences b/w means

- Proportions or rates, the rate ratio

→ *Cronbach's alpha is coefficient's of reliability or consistency. It is function of the number of test items and the average interco-relation among the items.*

Relationship b/w Incidence and Prevalence

- Prevalence = Incidence \times duration [$P = I \times D$]
- Longer the duration of the disease, the greater its prevalence. (e.g. in TB)
- On the other hand, if the d/s has high mortality, high case fatality, easily curability (very short duration) or acute conditions either because of rapid recovery or high no. of deaths, the prevalence rate will be relatively low compared with the incidence rate.

→ *Incidence is not affected by the duration of d/s. The use of incidence is generally restricted to acute conditions*

→ *Incidence is a rate. It is the no. of new cases occurring in a defined population during a specified period of time*

→ *But prevalence is a ratio. It includes all current cases (old & new) existing at a given point of time, or over a period of time in a given population.*

→ *Low prevalence of a d/s in community results \uparrow in no. of false positive cases.*

EPIDEMIC

- First case of an epidemic is called --- Primary case
- In case of an epidemic first thing to do--- Confirm the diagnosis.
- Important epidemics:
 - In 1955 ... Hepatitis E in Delhi
 - In 1994 ... Pneumonic plague in Surat

Response

- "The proportion of an exposed group that develops a specific effect" (dose-response relationship)
- Dose-effect relationship provides valuable information for the planning epidemiological studies & it helps the investigator to choose an appropriate effect to study.

Effect and related terminology

- Effect is the result of a cause. General term covering the impacts and result
- Effectiveness is a measure of the extent to which a

specific intervention, does what it is intended to do for a specified population. It is the extent to which a programme or intervention has made desired changes or has met its objectives.

- Effect measure** is a quantity that measures the effect of a factor on the frequency or risk of a health outcome.
- Effect modification** exist when the effect of a factor varies according to the level of another factor
- Efficacy** extent to which a specific intervention, produces a beneficial result under ideal conditions.
- Efficiency** is the amount of output against the input

→ *The most desirable method for measuring efficacy & effectiveness is the RCT.*

IMPORTANT DEFINITIONS

Objective

Is the precise statement about the end result of a program seeks to achieve. It is the **ultimate goal** towards which one is aiming while undertaking various activities and tasks. Measurable and attainable state.

Target

A defined or desired end result of specific public health activity to be achieved in a finite time. It represents measurable and attainable aims directed towards objectives.

Goal

"The intended outcome of a program not necessarily measurable in operational term". Goals are always statements about the health outcomes or status.

Mission

The purpose for which an organization exists

Learning

There are 3 types of learning

- Knowledge** ---Is cognitive component of learning
- Attitude** ---Is affective component of learning. Attitudes are acquired characteristics of an individual. Once formed attitudes are difficult to change.
- Skills** ---Is psychomotor learning

Attitude

A subjective probability judgement which describes the extent to which an individual considers a particular circumstance or relationship is true. Attitude is a/w emotional valence and is most likely to be influenced by motivation.

Opinion

A temporary, provisional view held by the people on a point of view

Beliefs

Are usually permanent, stable almost unchanging. These are usually derived from our parents, grand parents, and other people we respect. **Cultural Belief** is a learned behaviour which is relatively stable, consistent and permanent but liable to change

- *Habbits* : Accustomed ways of doing things e.g. hand washing before handling food.
- *Culture* : Learned behaviour which has been socially acquired.
- *Acculturation* : Culture contact

STEPS approach

- STEPS methodology deals with study of prevalence of **risk factors for non-communicable diseases** in a community
- STEP wise approach to Surveillance of NCD Risk Factors (STEPS) was developed by WHO as part of a global surveillance strategy in response to the growing need for country-level trends in **non-communicable d/s**. By using the same standardized questions and protocols, all countries can use STEPS information not only for monitoring within-country trends, but also for making between-country comparisons

Measurement of Disability

- **HBS scale** (Wing's comprehensive Handicaps, Behaviour and Skills schedule) is one of the most important way to assess the total child population in terms of detailed scales of specific abilities and disabilities
- Disability Assessment schedule (**DAS**) is being used in several communities as a source of high quality routine data for total population
- International Classification of Impairment, Disability, and Handicap (**ICDH**) aimed to provide a unified and standard language to frame a reference for the "consequences of health conditions"
- **IDEAS**: Mental disability was assessed by Indian Disability Evaluation and Assessment Scale (IDEAS), a scale for measuring and quantifying disability. In IDEAS disability

is calculated on the basis of self-care, interpersonal activities, communication and understanding, job work

- International Classification of Functioning, Disability and Health commonly known as **ICF**, is a WHO framework for measuring disability at both individual and population level

'Targeted intervention'

- It combines comprehensive and integrated approach
- Started with a basic purpose of reducing **HIV** transmission in most vulnerable population.
- Targeted group include --- i.e. sex workers, Intravenous user of drugs (IUDs), homosexual men, migrant labourers, and street children
- The main activities are
 - T/t of STDs, provision of condoms
 - Behavioural change communication
 - Creating an environment that will promote behaviour change

Purchasing power parity (PPP)

PPP is defined as the no. of units of a country's currency required to buy the same amount of goods and services in the domestic market as one dollar would buy in the USA. In 2001 India's per capita GNP has been estimated at \$ 2450 (PPP).

OSHA guidelines

Occupational Safety and Health Administration (OSHA) guidelines are recommendations for **infection control in hospitalized individual**.

- Mercury is best disposed off by --- Safe collection and recycle
- Licences for blood banks in India are issued by --- Drugs and controller general in India
- Pharmacovigilance is a/w --- Monitoring of drug safety
- Counterfeit medicine is --- if a drug is produced with an intention to cheat

EPIDEMIOLOGICAL INDICATORS/ MEASUREMENT OF MORTALITY AND MORBIDITY

Secondary attack rate (SAR)

- Number of exposed persons developing d/s within the range of longest i.p. following the exposure to primary case"

$$\frac{\text{No. of exposed persons developing d/s within the range of longest i.p.}}{\text{Total no. of exposed or susceptible contacts}} \times 100$$

$$\frac{\text{Secondary case within i.p.}}{\text{Susceptibles [total child - (immunized + primary case)]}} \times 100$$

- Used to assess **communicability** of d/s (e.g. SAR of pertussis > measles)
- Calculated on the basis of **maximum incubation period**

Relative Risk (RR)

- Incidence of disease among exposed to that among non-exposed.
- Important to clinicians

$$= \frac{I_E}{I_{NE}}$$

Attributable Risk (AR)

$$AR = \frac{I_E - I_{NE}}{I_E}$$

Case Fatality Rate (CFR)

- Represents **killing power / virulence of disease**.
- It is simply the proportion of deaths to cases.
- The time interval is not specified.
- Used in acute infectious diseases. CFR indicates severity of acute disease.

$$CFR = \frac{\text{Total no. of deaths due to particular disease}}{\text{Total no. of cases due to same disease}} \times 100$$

Standardized Mortality Ratio (SMR)

- Ratio** of observed deaths to expected deaths expressed as percentage
- It permits adjustment for age and other factors
- Simplest and most useful form of indirect standardization

- Best method to compare vital statistics of two population is age standardized death rate
- While analyzing a data, allocation into similar groups is done to ensure comparability

- Crude mortality rate (CMR or CDR)** : Total number of deaths divided by estimated mid year population per 1000.

Proportional MR

- Simplest measure to estimate the burden of a d/s in a community. (e.g. CHD causes 25-30% of all deaths in most western world)
- It indicates the *magnitude of preventable mortality*

Adjusted / standardized rates

- Age adjusting rates is a way to make fairer comparisons between groups with different age distributions. Rates are also adjusted according to races, genders, or time periods.
- A "standard" population distribution is used to adjust death and hospitalization rates. The age-adjusted rates are summary measures adjusted for differences in age distributions.
- Direct standardization is used to compare mortality rates b/w 2 countries. This is done because of the difference in age distributions.

Basic Reproductive Rate (BRR)

BRR of an infection is primarily dependent upon length of time the primary case is infectious to others.

Important Terminology

D/s	Example
Contagious	Scabies, trachoma, STDs, leprosy, syphilis
Holoendemic	Malaria (Affects mainly infants/children)
Pandemic	Influenza (1918), Cholera el tor (1962), Ac hemorrhagic conjunctivitis
Exotic	D/s imported. Yellow fever in India, Rabies in Australia/ USA
Hyperepidemic	D/s is present in high incidence & prevalence, affects all age

- Bimodal peak of d/s (bimodal incidence curve) or bimodal age distribution is seen in ---
Hodgkin's lymphoma, leukemia, nasopharyngeal carcinoma and female breast carcinoma.
- Ring immunization is given for 100 yards of a detected case.
E.g. in small pox & measles
- Chemical isolation is rapid t/t of cases in their own homes and rendering them non-infective as quickly as possible. (E.g. in STDs, TB, leprosy)

Short term fluctuation (in time) of disease / epidemics

Type	Subtype	Feature
Common source	Point source, single exposure	Median i.p. is important, All cases develop within one IP, Symptoms start at same and abrupt ending (explosive) Examples : No 2 ^o waves Food poisoning, Bhopal gas tragedy, Minimata d/s, Chernobyl tragedy
	Multiple/ repeated source, continuous exposure	- Gonorrhoea (CSW) - Legionnaire's d/s - A well of contaminated water -
Propagated		Infectious origin (Polio Hep A), via arthropod (plague) Cases develop later than IP, Slow transmission in areas with good herd immunity, 2 ^o waves always SAR is high

Periodic Fluctuation /Trends

Seasonal	Cyclic	Secular
Seen in most communicable d/s - Measles, Rubella - Varicella - Hay fever - Gastroenteritis - Cerebral meningitis	Cycles spread over short period of time - Measles (2-3 yearly) - Rubella (6-9) yearly in pre vaccine era - Influenza pandemic	In coronary HD - Lung cancer - T.B. - Polio - Typhoid - DM - Diphtheria
Related to environmental conditions (vector-dynamics)	Occur d/t naturally occurring antigenic variations in the level of herd immunity (antigenic variations), Related to seasonal variation & migration	Changes in the occurrence of ds over a long period

Iceberg phenomena is seen in

Leprosy, HTN, DM, PEM, polio, Influenza, Hepatitis

Infectious diseases whose control is solely based on active immunization

- Diphtheria
- Polio
- Tetanus
- Measles

Incubation period of some diseases

Diseases with very short i.p. (hrs to 2-3 days)	<u>Staphylococcal food poisoning (6hrs)</u> Bacillus cereus (1-6 hr emetic type, 1-2 day diarrhoea type) Gas gangrene (<3 d) Influenza, anthrax (1-3 d) Cholera (2 d) Bacillary dysentery (1-7 d) Tularemia (1-7 d) Diphtheria, plague (2-5 d) [Mnemonic: BBC AT D PGI Seminar]
Median length i.p. (10 days - 3 wks)	Viral diseases (Chicken pox, measles, mumps) <u>Pertussis (7-14 d)</u> Typhoid (10-14 d) <u>Mumps (14-21 d)</u> Tetanus (3-21 d) [Mnemonic: P ₂ M ₂ T ₂]
Longer i.p. (Months to years)	Rabies T.B., Leprosy Slow virus ds Kala-azar (1-3 mo) Filariasis (5-8 mo) Elephantiasis (10 yrs.)

Both active & passive vaccination can be given together

- Diphtheria
- Hepatitis B
- Tetanus
- Rabies (but NOT for measles)

Isolation has distinct value in

- Diphtheria
- Cholera
- Pneumonic plague
- Streptococcal respiratory diseases

Soil acts as a reservoir for the agents of following infectious diseases

- Mycetoma
- Anthrax
- Coccidiomycosis
- Tetanus

Only human being are reservoir for

- Measles
- Salmonella (Typhoid)
- Hookworm
- Amebiasis

- Leishmaniasis in India
- Cholera

Dead - end infections (Man is dead end host for---)

- Rabies
- Plague (Bubonic)
- Tetanus
- Trichinosis

Latent infection occurs in

- HSV
- Ancylostoma
- Slow virus infections
- Brill-Zinsser disease

D/s infective during later part of incubation period.

- Whooping cough (pertussis)
- Measles
- Chickenpox
- Hepatitis A

- Carriers are not known to occur in : Measles
- Subclinical infection is not seen in : Measles
- Herd immunity is not important in : Tetanus
- Isolation is not useful in : Polio, Hepatitis A, typhoid fever (Not practiced in)
- Maternal antibody are not protective Vs : Pertussis

Transmission of arthropod borne disease

Biological

Propagative	No cyclic change, only multiplication	Cycle of Plague bacilli in rat flea, Yellow fever virus in aedes
Cyclo-propagative	Disease agent undergo cycle + multiplication	Cycle of Plasmodium in anophles (malaria)
Cyclo-developmental	disease agent undergo cycle + no multiplication	Cycle of Dracunculiasis (guineaworm), filariasis

Direct contact

Man to man transmission is seen e.g. Scabies, pediculosis

Mechanical

Mechanical transmission by arthropod e.g. Housefly

- D/s which is globally transmitted by anopheles, aedes, and culex mosquitoes --- Filariasis.
- Airborne transmission occurs by dissemination of airborne droplet nuclei (small particle residue of size $\leq 5 \mu\text{m}$) containing microbes. E.g. Measles virus, VZV, TB bacilli.
- Contact transmission is the m/c route of transmission of health care associated infections.

Case notification under IHR

- Cholera
- Plague
- Yellow fever
- Small pox
- Polio
- Influenza
- SARS

D/s which are notifiable to WHO and also subjected to IHR / International surveillance

- Louse borne typhus
- Relapsing fever
- Malaria
- Salmonellosis
- Polio
- Influenza (Viral)
- Rabies
- [mnemonic : MR₂.SLIP]

Transovarian transmission is seen in -

Tick and mite born d/s (but it is not seen in louse, flea)

- Yellow fever (\pm)
- Dengue
- Scrub typhus (mite)
- Rickettsial pox (mite)
- Rocky mountain spotted fever
- Indian tick typhus
- Q- fever

Types of carriers

Incubatory	Convalescent	Healthy	Chronic
Measles	Cholera	Polio	Malaria
Mumps	Diphtheria	Salmonellosis	Gonorrhea
Polio	Dysentery	(Typhoid marry)	Meningitis
Hepatitis B	Typhoid	Cholera	Typhoid ($\geq 1\text{yr}$)
Diphtheria	Pertussis	Diphtheria	Dysentery
Influenza	(whooping cough)	Meningitis	HBV ($\geq 6\text{mth}$)
Measles			
Pertussis			

Mnemonic to remember -

Consider only capital or underlined letters

1. (M³y PHD is IMP) is for incubatory carriers
2. (Water Chlorination & DDT) & for convalescent carriers
3. (PSM Defines Cholera & health) h for healthy carriers
4. (Chronic carriers Traveling in DH of MGM)

Some Important Definitions

Screening time

Interval b/n 1st clinical detection & final critical point

Lead-time

Time lag b/n 1st possible detection & usual time of diagnosis.

Serial interval

Gap in time b/n onset of primary & secondary case.
(measures incubation period)

Generation time

Time interval b/n receipt of infection & maximum infectivity of host

Period of surveillance (quarantine)

Equal to maximum I.P.

Primary case

1st case of a communicable disease introduced into population unit which is studied (in an epidemic), which may or may not come to an observer's attention.

Index case

1st case to come to attention to investigator

Latent infection

During which infectious agent is not shed or not demonstrable in blood / tissue

Ex: HSV, Brill-Zinsser disease, ancylostoma, slow virus d/s.

Pseudo-carrier

Carriers of avirulent organism

Incubation period

Time interval b/w invasion of infectious agent & appearance of first sign/symptom.

Isolation

Restriction of infected person for the period of communicability.

VACCINES AND IMMUNIZATION

Safety of Vaccines in pregnancy

Safe

- Polio (give IPV if immediate protection is required)
- Yellow fever
- Inactivated viral vaccines (eg. Hepatitis B, HAV, Influenza, Pneumococcal), Rabies may be given during 2nd & 3rd trimester, if needed.
- Diphtheria toxoid, Tetanus toxoid

Contraindicated

- Most of the live viral vaccines
 - Measles, Mumps, Rubella, MMR
 - Varicella
 - BCG / Tuberculin
- Meningococcal (killed) vaccine

- Breast feeding does not adversely affect the immune response & is not a contraindication for any vaccine
- Measles vaccination is NOT recommended in elderly.

In HIV positive symptomatic pt (In AIDS)

Safe

- Other recommended vaccines - M, M, R, MMR, HBV, DPT
- IPV in special situations
- BCG (in asymptomatic pt / in Indian set up)
- H. influenzae (inactivated vaccine)
- Quadrivalent meningococcal vaccine
- 23 valent pneumococcal vaccine.

Contra indicated

- Chicken pox vaccine (VZV)
- Rota virus vaccine
- Polio (OPV)
- BCG in symptomatic HIV⁺ pt.
- Yellow fever vaccine (live)
- Typhoral

- ➔ According to Nelson's MMR and varicella can be given to HIV infected children who are not severely immunosuppressed
- ➔ Live attenuated vaccines are usually contraindicated in immunodeficiency states, including those with congenital immunodeficiencies & on immunosuppressive t/t because d/s can flare up. However measles can be given

Immunoglobulins

Human Ig		Non-human Ig (antisera)	
Human normal Ig	Human specific Ig (Hyper immune)	Bacterial	Viral
Hepatitis A	Chicken pox P _x (VZV)	Diphtheria	Rabies
Tetanus	Hepatitis B	Tetanus	
Measles	Rabies	Gas gangrene	
Mumps	Tetanus P _x in wound	Botulism	
Rubella	Anti-D immunoglobulin		

Contraindications to Vaccines

- In < 2yr : Typhoid, Meningococcal, Pneumococcal (In < 1yr : YF is also contraindicated)
- In fever : Typhoid
- In progressive neurological illness: DPT
- In pregnancy : Live vaccines (except YF, polio)
- Patient on steroid therapy, immunosuppression, immunodeficient children : Live vaccines
- Chronically ill, immunosuppressed & those at risk of infection with capsular organism (splenectomized, multiple myeloma patient) should receive pneumococcal vaccine
- Above group + terminal complement deficiency patient should also receive quadrivalent meningococcal vaccine.
- Live vaccines are contra-indicated in immunodeficient children except measles
- Ideally live attenuated vaccines should not be co-administered with immunoglobulins.
- Vaccine and Ig can be co-administered for yellow fever, polio & hepatitis B
- 2 Live vaccines can be given simultaneously but at different sites.
- YF and cholera vaccine should NOT be given together.
- Active & passive immunity may be given simultaneously for Diphtheria, Rabies, Tetanus, HBV but not for measles. [DR-TB]

Efficacy

- Tetanus 100%
- HBV, MMR ~ 100 %
- Diphtheria 95 %
- Measles 85 %
- Pertussis 80%
- D,P,T 3 doses 95%

Reconstituted vaccines

- BCG, Measles, Yellow fever are example of freeze dried vaccines. They should be reconstituted before use
- *Max^m time for use of reconstituted vaccines*
Yellow fever within ½ hr, measles within 1-4 hr, and BCG vaccine should be used within 3 hrs.
- *Thermostability*
Plain TT > Freeze dried BCG > DT > DPT > Hep B > Measles > OPV > YF > Reconstituted BCG

Vaccines addendum

- DPT contain thiomersol (preservative)
- OPV contain MgCl₂ (thermostabilizer)
- Measles vaccine contain neomycin & erythromycin (preservative)

Strains of vaccines

- BCG Vaccine
 - Bacille Calmette Guerin : Was the 1st strain developed from bovine strains of M. tuberculosis.
 - WHO recommends "Danish 1331" strain for production of BCG vaccine. Since Jan.1967 Guindy Lab at Chennai has been using it.
 - PPD ,T-23 & Tween-80 are used for tuberculin testing. 1 tuberculin unit (TU) is equal to 0.01 ml of OT or 0.00002 mg of PPD
- Measles vaccine
HDC-Edmonston-Zagreb strain is used. It provides protection to the children from 4 to 6 months onwards.

Heat sensitivity of vaccines

- Storage temperature for most of the vaccines is +2°C to 8°C.
- At the health centres most vaccines (except polio) can be stored up to 5 weeks if the refrigerator temperature is strictly kept between 4-8°C
- OPV is the highly heat sensitive vaccine. OPV (- 20°C) and Yellow fever (-30 to -5 °C) should be kept in freezer compartment
- Other vaccines which are maintained at cold temperature but never allowed to freeze are
BCG (2-8°C) > DPT, TT, typhoid, diluents (4-8°C)
- **Reverse cold chain:** It is the maintenance of optimum cold temperature during transport of vaccine from periphery to the laboratory for potency testing as in OPV (also useful for transport of stool samples).
- Vaccine vial monitors (VVM) are used for potency testing of OPV

Killed (inactivated) vaccine

- Rabies
- KFD
- Salk (IPV)
- Influenza
- JE
- HBV
- Plague

[mnemonic **KRISH** kills Jojo]

Live (attenuated) vaccine

- BCG
- Typhoid: oral (Ty 21a)
- Polio: oral (OPV)
- Yellow fever (17D)
- Epidemic typhus
- VZV (chicken pox)
- M, M, R

Proposed Changes in NIP 2009-2010

- DT booster to be replaced by DPT
- DPT and Hep B at 6, 10, 14 weeks to be replaced by DPT + Hep B + Hib pentavalent vaccines

Cell-fraction derived vaccines

- Meningococcal vaccine from *polysaccharide antigen of cell wall*
- Pneumococcal vaccine from *polysaccharide capsule*
- Hepatitis B vaccine from *polypeptides*

Combined Vaccines

- MMR : Measles + mumps + rubella
- MMRV : Measles + mumps + rubella + varicella
- Pentavalent vaccines
 - DPT + Hep B + Hib (Easy five)
 - DPT + Hib + IPV (Pentaxim), Hep B given in other thigh
- Conjugated Pneumococcal vaccine is 23 valent vaccine.

→ Active immunization includes --- Live/ killed vaccines, toxoids.

→ Immunity transferred from mother to fetus --- Passive / innate immunity.

→ Adsorbant used in DPT vaccine is --- Aluminium phosphate or aluminium hydroxide

→ DPT may be given in non-progressive neurological disorders
But DPT & pertussis vaccines are not given to a child with progressive neurological illness

(Acellular pertussis vaccine can be used instead of conventional DPT).

→ Febrile seizures and family history of convulsions are not contraindications for DPT vaccination. Give paracetamol soon after injection in such cases to prevent fever.

→ Anaphylaxis can occur with any vaccine. Immediate t/t is inj. adrenaline.

Newer Vaccines

◦ JE Vaccine

- JE vaccine is recently recommended and is approved by MOHFW for immunization in selected highly endemic zones of the country.
- Strain used is SA -14-14-2 to be given at the age of 16-24 months along with DPT/ OPV.

◦ HPV Vaccine

- Vaccine with high efficacy
- As the cervical cancer is an important cause of morbidity in developing world, this vaccine is gaining popularity
- 2 Vaccines are available --- Gardasil is quadrivalent (contains HPV strains 6,11, 16,18), Cervarix is bivalent (16,18)

◦ Rota virus Vaccine

- Vaccines available are : Rotashield, Rotateq & Rotarix
- Administered orally in a 2 dose schedule. First dose should be given <12 week and 2nd dose < 24 week. Minimum interval b/w 2 doses should be 4 weeks
- Ad/c observed with Rotashield : Intussusception

→ Dukoral is a monovalent inactivated vaccine. It protects against travellers' diarrhea caused by *E. coli* as well as from cholera.

Pulse Polio Immunization (PPIs)

- PPI was started on 9th December 1995.
- 2 drops of OPV are given to all children 0-5 years of age, in the country on a single day, regardless of previous immunization. PPI is carried out on 'national immunization days' (NIDs) every year in December & January.
- Pulse stands for "polio under lameness survey eradication".
- The dose of OPV during PPIs are extra doses which supplement, and do not replace the routine dose.
- A country will be declared polio free only when no new cases will be reported for 3 consecutive years.
- Since 2000, India has exceeded the WHO established AFP surveillance targets, i.e. a non polio AFP rate of > 1 per 10,000 population aged < 15yrs & adequate stool specimens taken from > 80% AFP cases.
- Type 1 causes most number of polio cases.
Type 2 is most effective antigen (most immunogenic)
Type 3 is responsible for max^m no. of VAPP but smaller epidemics.

IPV Vs OPV

IPV / Salk	OPV / Sabin
Killed formalized	Live attenuated, trivalent
Administered s/c or i/m	Orally
Induces humoral immunity	Induces both local and systemic (intestinal + humoral) immunity
It prevents paralysis only, not re-infection	Prevents paralysis + intestinal re-infection
Not useful in epidemics	Useful in epidemic
4 doses required	3 doses required
(Booster with OPV can be given)	More chance of VAPP

Immunization schedule for children not immunized at infancy

- If an unvaccinated infant is brought first time at the age of 9 months then he should receive -- BCG, DPT₁, OPV₁, HepB₁ (& measles vaccines also if compliance is the problem)
- If an unvaccinated child is brought first time b/w the age of 1-2 years then he should be given --- DPT₁, OPV₁, HepB₁, MMR (BCG vaccine is not recommended after 1 year now a days)
- If only one vaccine has to be given to an unimmunized infant at 9 month of age measles is most important. Similarly b/w 1-2 year of age MMR is most important vaccine.
- Typhoid (V₁) vaccine can be given after the 2 years of age either orally (Ty21a, typhoral) or as injectable vaccine

Vaccines recommended for Elderly

- Influenza : annual
- Pneumococcal: at least once
- Tetanus: every 10 years

Adverse effect of different vaccine

- Incessant cry, hypotensive hyporesponsive episodes --- DPT
- TSS (Toxic shock syndrome) --- Measles
- Lymphadenitis --- BCG
- Sterile abscess --- T-series vaccine
- Seizures --- DPT, Measles
- Intussusception --- Rota virus vaccine

- Anaphylaxis, bacterial abscess, local reaction --- Any vaccine

- GBS: following swine influenza vaccination
- SSPE: A very rare complication of measles vaccination
- Post vaccination encephalitis: after rabies, small pox vaccination.
- TSS can occur d/to contamination of staph.aureus in the multidose measles vaccine vials. To prevent this c/c reconstituted measles vaccines should be used within 3-4 hours only.

Individual Vaccines

- Freeze dried vaccine is BCG
- Lyophilised vaccines are : Measles, MMR, Varicella, Meningococcal, JE, rabies.
- An example of split genome/ split virion vaccine : Influenza vaccine, Rotavirus .

INFECTIOUS DISEASES**Mode of Transmission of some Diseases****Airborne transmission via Droplet nuclei**

Transmission occurs by dissemination of airborne droplet nuclei (< 5 µm)

- Measles (Rubeola) virus
- Chicken Pox
- Tuberculosis

Droplet transmission

N95 or higher respirator masks should be used (droplet precautions) for following d/s.

- Viruses : adeno, influenza, mumps, parvo B19, rubella, SARS, swine flue,
- Pharyngeal diphtheria, pertussis, Hib, streptococcal pharyngitis, pneumonia, plague, mycoplasma, Neisseria

Contact Transmission

M/c route of transmission of health-care associated infectⁿ

- Direct contact transmission : Whooping cough, staphylococcal infections (impetigo)
- Indirect contact transmission

Feco-oral

- HAV, Enteroviruses
- Enteric fever (typhoid), cholera, poliomyelitis

Vaccine	Type/Strain	Content/dose	Diluent	Schedule	Dose, Route	Protective Efficacy	Contra-indication	Ad/E	Storage
BCG (Freeze-dried)	Live Attenuate vaccine (LAV) Bacillus-calmetai guerin bovine strain	0.1 to 0.4 million viable mycobacteria	Normal saline	single dose at birth or at first contact	0.1 ml Intradermal left deltoid	0-80%	Immunodeficiency AIDS	Axillary Lymphadenitis	+2°C to +8°C
DTP_w (Whole cell vaccine) DTP (Acellular vaccine)	Diphtheria and tetanus-toxoids P _w . Killed whole cell pertussis P ₂ . Highly purified pertussis components	Diphtheria toxoid- > 20 to < 30 Lf Tetanus toxoid > to < 25 Lf P _w - > 4 IU P _a - 3 to 5 mcg each of five purified pertussis antigens	None (Liquid form)	3 Primary doses at 6, 10, 14 wks Boosters at 18 months and 5 years	0.5 ml, i/m Anterolateral aspect of thigh	Pertussis 85% Diphth- 95% Tetanus 100%	Progressive neurological disease Severe reaction to first dose Incessant cry Rarely encephalopathy	Fever Local pain and induration (Milder with first dose) Rarely encephalopathy	+2°C to +8°C
OPV	LAV (Sabin strain grown in PMK cells)	Type 1-10 ⁵ CCID ₅₀ Type 2-10 ⁵ CCID ₅₀ Type 3-10 ⁵⁻⁸ CCID ₅₀	None (Liquid form)	Primary doses at birth, 6, 10 14 wks Boosters at 18 months and 5 years	2 drops oral	80-90%	Immunodeficiency HIV disease Contanets of immunodeficient	VAPP rarely	-20°C or below
Hepatitis B	Genetically engineered recombinant subunit vaccine	10 mcg of purified BHsAg	None (Liquid form)	Birth, 6, 14 wks. If not given at birth -6, 10, 14 wks. Or 0, 1, 6 mo.	0.5 ml, i/m Anterolateral aspect of thigh	90%	None	Local pain and erythema	+2°C to +8°C
H. Infl. B PRPD or PRPT or HbOC	Conjugate capsular polysaccharide-b vaccine	10 mcg of capsular polysaccharide	None (Liquid form)	3 Primary doses at 6, 10, 14 wks, Boosters at 15-18 months	0.5 ml, i/m Anterolateral aspect of thigh	90-100%	None	Local pain and erythema Mild fever	+2°C to +3°C
Measles (Lyophilised)	LAV Edmonston-Zagreb strain grown on human diploid cells	1000 CCID ₅₀ of measles virus	Sterile water	Single dose at 9 months	0.5 ml, s/c Deltoid/Thigh	95%	None	Mild fever Mild rash after 7 days	+2°C to +8°C
MMR (Lyophilised)	Trivalent LAV Measles as above Mumps-L-Zagreb strain Rubella-Wister RA 27/3 strain	Measl. 1000 CCID ₅₀ Mumps-5000 CCID ₅₀ Rubella-1000 CCID ₅₀	Sterile water	Single dose at 15 months	0.5 ml, s/c Deltoid/Thigh	95%	Systemic hypersensitivity to neomycin	Mild fever Mild rash after 7 days	+2°C to +8°C
Varicella (Lyophilised)	LAV Oka strain grown on human diploid cells	10 ^{3.3} PFU of varicella virus	Sterile water	1-12 Yrs. Single dose ≥ 13 Yrs. -2 doses at 1 mo interval	0.5 ml, s/c Deltoid	95-100%	Systemic hypersensitivity to neomycin	Milder varicella type rash (≤ 10 lesions) in first 3 wks. Fever	+2°C to +3°C

Hepatitis A	Formaldehyde inactivated HIM 175 antigen	720 ELISA units of viral antigen	None (Liquid form)	After 1 year 2 doses at 6 months interval	0 ml, i/m Anterolateral aspect of thigh	90-100%	None	Local pain and erythema	+2°C to +8°C
Typhoid Vi antigen vaccine	Inactivated capsular polysaccharide (Vi) vaccine	30 mcg of inactivated Vi capsular polysaccharide	None (Liquid form)	First dose after 2 years Booster every 3 years	0.5 ml, i/m Deltoid	70%	None	Mild local reaction	+2°C to +8°C
Meningococcal (A+C) (Lyophilised)	Inactivated capsular polysaccharide vaccine	50 mcg each serotype of inactivated capsular polysaccharide	Sterile water	2 years and above during epidemics	0.5 ml i/m or s/c Deltoid/Thigh	90% against the covered strains	None	Mild fever Local reaction	+2°C to +8°C
Japanese encephalitis (Lyophilised)	Killed viral vaccine Mouse brain Nakayama NIH strain	< 2 ng/ml of myelin basic protein	Sterile water	Routine use in high-risk areas Two doses at 1 mo interval for children > 1 yr Booster every 3 yrs	1-3 yrs: 0.5 ml > 3 yrs: 1.0 ml s/c Deltoid	80-90%	Hypersensitivity to first dose	Local reactions Allergies Rarely encephalitis	+2°C to +8°C
Pneumococcal 23 valent vaccine	Inactivated capsular polysaccharide	25 mcg each serotype of inactivated capsular polysaccharide	None (Liquid form)	Single dose for high risk children > 2 yrs	0.5 ml, i/m or s/c Deltoid/Anterolateral thigh	80%	None	Local reaction	+2°C to +8°C
Influenza	Inactivated (split virion) vaccine	7.5-15 mcg of each of the chosen strain	None (Liquid form)	Single dose after 6 mo when indicated Revaccinate every year with strain adjusted vaccine	6 mo-3 yrs: 0.25 mL > 3 years-0.5 ml i.m. Deltoid/Anterolateral thigh	80-90%	Egg allergy	Local reaction	+2°C to +8°C
DPT _w ⁺ Hepatitis B combination	Same as for* individual vaccines	Same as for* individual vaccines	None (Liquid form)	3 doses at 6, 10, 14 wks	0.5 ml, i.m. Anterolateral aspect of thigh	Same as* for individual vaccines	Same as for* individual vaccines	Same as for* individual vaccines	+2°C to +8°C
DTP _w ⁺ Hib combination	Same as for* individual vaccines	Same as for* individual vaccines	DPT _w vaccine to be added to lyophilised	3 doses at 6, 10, 14 wks	0.5 ml, i.m. Anterolateral aspect of thigh	Same as* for individual vaccines	Same as for* individual vaccine	Same as for* individual vaccine	+2°C to +8°C
Rabies (Lyophilised)	Tissue culture inactivated vaccines Rabies virus grown in HDCV-human diploid cells PCEC-chick embryo cells VERO cell-vero cell	> 2.5 IU of inactivated rabies antigen	Sterile water	Any age Pre-exposure Three doses on day 0, 7, 28 Post-exposure Five doses on day 0, 3, 7, 14, 28	1.0 ml, i.m.	90-100%	None	Local	+2°C to +8°C

* same as for individual vaccine; LAV Live attenuated vaccines; PFU Plate Forming Units.

- Q-fever is transmitted by --- Inhalation of *C. brunetii* in aerosols
- Dracunculiasis is transmitted by --- Consumption of water containing cyclops harbouring Guinea worm
- Hookworm is transmitted by --- Direct penetration through skin.

Period of infectivity

- In Diphtheria 14 to 28 days (2 to 4 weeks) from onset of disease (Isolation 3 days after Tetracycline started)
- In Chicken pox 2,5 (2 days before appearance of rash & 5 days after rash)
- In Measles 4,5 (4 days before ————5———)
- In Rubella & Mumps 7,7 (7 days before ————7———)
- In Whooping cough 7,21 (1 week of exposure to 3 week after onset of paroxysmal stage).

In whooping cough (Pertussis) patient is most infectious during catarrhal stage and isolation is recommended for 4 weeks or until paroxysm ceases)

[Mnemonic DCM RMP = 24, 25, 45, 77, 77, 721]

Period of isolation

- In salmonellosis isolation is recommended till 3 consecutive stool cultures are negative
- In MUMPS isolation is recommended until swelling subsides
- Isolation of the patient as a measure to prevent disease among contacts is **not** very useful for --- Hepatitis A

Drugs for chemoprophylaxis

- | | |
|----------------------------------|-----------------------|
| Bact. conjunctivitis, pertussis, | |
| Diphtheria | --- Erythromycin |
| Plague, cholera | --- Tetracycline/Doxy |
| Meningococcal meningitis | --- Rifampicin |
| Influenza | --- Amantadine |
| Tetanus | --- Penicillin |
| Leptospira | --- Doxy |

→ Chemoprophylaxis is **NOT** used in measles, typhoid, scabies.

→ Chemoprophylaxis for diarrhoeal d/s in case of disaster --- Doxy

Rural Urban variations of d/s

- D/s more frequent in urban areas --- Chronic bronchitis, accidents, lung cancer, CVD, mental illness
- D/s more frequent in rural areas --- skin d/s, zoonoses, helminthiasis

- Rural urban variation of d/s is **NOT** seen in --- TB

SMALL POX

- S~ was eradicated on 8th May, 1980.
- Edward Jenner discovered first vaccine, which was against small pox.
- Small pox was eradicated becoz :
 - There was life long immunity after d/s,
 - Pt with subclinical infection did not transmit the d/s,
 - No known animal reservoir,
 - No known long term carrier,
 - It was easy to diagnose cases,
 - Vaccine was highly effective.

MEASLES (Rubeola)

- Measles virus is a RNA para-myxovirus. It can not survive outside the human body for any length of time.
- Only infects human beings. (incidence is equal in M = F)
- > 80% SAR among susceptibles
- The only source of infection is a case of measles. Carriers are not known to occur
- Most infection are clinical (sub-clinical infection not seen)
- Immunity develops 11-12 day after vaccination & persist throughout life.
- To eradicate measles % of population to be vaccinated is at least 95%.
- M/c complication otitis media.
- M/c cause of mortality diarrhoea.

CHICKENPOX (Varicella)

- Rash is **pleomorphic** (all stages of the rash i.e. papules, pustules, vesicles, may be present at one time).
" Dew drop on rose petal" is characteristic of rash.
- Reactivation occurs in 10-30% results in **Shingles (Herpes zoster)** which is most common late complication.
- Lesions are highly contagious until crusting occur.
- SAR is 90%.

RUBELLA

- Caused by Rubivirus (ss RNA virus)
- It produces mild fever enanthem, mild rashes noticed on the 3rd day of fever and characteristic posterior auricular, post-cervical and occipital adenitis.
- It is also k/as "three day measles" because the rashes appear on 3rd day of fever.
- The I.P. is 14-21 day. Rashes clear by the 3rd day rashes may be -nt in some cases.
- Adult women may develop purpura and arthritis.

- Enanthem consist of discrete rose colored spots over soft palate (**Forchheimer's spots**).
- Infective period is 7 days before and 7 days after exanthem.
- Target to protect from rubella--- 15-39 yr female (first)> 1-4 yr children > infant.

Congenital Rubella

- Congenital defects occur in 90% of infant whose mother acquire maternal infecⁿ before the 11th week of pregnancy, So risk of fetal damage is maximum in **first trimester**. In Rubella M/c congenital defects are **deafness**, cardiac malformations (esp. **PDA**) and cataracts.
- Other effects are --- LBW / IUGR, salt-pepper chorioretinitis, cerebral palsy, mental retardation.

MENINGOCOCCAL MENINGITIS

- Case fatality rate of untreated cases is 80%
- Carriers are most important source of infection (temp. carriers of 10 month)
- Methods of Prevention and control:
 R_x of cases : **Penicillin (DOC)**
 R_x of carriers : **Rmp**
 DOC for chemoprophylaxis of contacts : **Rmp**
- Mass chemoprophylaxis — **Ciprofloxacin & Minocycline**
- Isolation is not very useful
- Vaccine available against A,C,Y, W -135 (but not against type B). It provides immunity for 3 yrs. Type B is most dangerous.
Not recommended for the use in <2 years and is contraindicated in pregnant women.

PERTUSSIS

- Only infect man, so the source of infection is only man.
- 90% SAR (communicability very high)
- No cross immunity with parapertussis
- **No sub clinical infection & No carrier state**
- Incubation period 7 - 14 days
- Maternal antibodies do not protect infants against pertussis (so infants are susceptible from birth)
- C/c :- bronchitis, bronchopneumonia, bronchiectasis [3'B']
- R_x :- Cases :- erythromycin is DOC
- Prophylaxis:- Contacts :- **erythromycin** is DOC
 - All infants DPT at 1½ mth, 2½ mth, 3½ mth
- Infective period 3 wks after onset of paroxysm
- Catarrhal stage most infective
- Absolute lymphocytosis is characteristic in late catarrhal or paroxysmal stage.

DIPHTHERIA

- Carriers may be temporary/chronic
- *Nasal carriers are dangerous* than throat
- *Nasal D~ is mildest form but most infectious*
- **Immunization does not prevent carrier state.**
- Prophylaxis of suspects : **anti-toxin**
 R_x cases / carriers : erythromycin x 10 days
 Prophylaxis of non-immunized close contacts :- **erythromycin**
 R_x contacts which are vaccinated⁺ / booster given within two years - **no action**
 R_x contacts which are vaccinated⁺ / booster given >2 years - **single booster DT (Diphtheria tetanus)**
- *Infectivity : 14 - 28 days after onset of d/s (or two throat culture are -ve)*
- *Faucial / pharyngo-tonsillar form is most common while laryngo - tracheal form is most severe.*
- Characteristic swollen neck k/as "Bull neck" d/to enlarged anterior cervical lymph nodes.
- C/c : Myocarditis → arrhythmias (m/c cause of death), CN & PN palsies leading to palatal paralysis.
- M/c nerve paralysed in diphtheria -posterior pharyngeal, laryngeal, and facial nerves.

RABIES

- Prodromal stage f/b pain & tingling at site of bite is the only symptom in 80% of cases
- Stage of CNS excitation → sensory → motor → sympathetic system are involved in that order
- O/E : pupils dilated, reflexes ↑ed. **Hydrophobia** is pathognomonic.
- D/g : Confirmed by **antigen detection** using immunofluorescence of skin biopsy.
- *Nervous tissue vaccine:* Grown in brain of sheep (**Simple vaccine**)
 - Demerits: - Low potency, fatal reaction, large no. of doses required
 - Suckling mouse brain devoid of neuromuscular effect
- *DEV:* risk of allergy
- Australia is Rabies free country.
- *Cell derived vaccine:* **HDCV** derived from human fibroblasts
 2nd generation tissue culture vaccines are derived from "vero cells"
- Neutralizing antibodies are present in serum / CSF after 8th d. Their presence in blood of man & animal is considered an index of protection against infection with rabies virus.

c Street virus Vs Fixed virus

Street virus	Fixed virus
<ul style="list-style-type: none"> Virus recovered from naturally occurring cases of rabies Long & variable I.P. (20-60 d in dogs) Forms "Negri bodies" in neurons of brain and multiply in extra-neural tissues 	<ul style="list-style-type: none"> Virus recovered after serial brain to brain passage of street virus in rabbit Short & fixed I.P. (4-6 d) Does not form Negri bodies & no longer multiply in extra neural tissues so it is used for <u>vaccine production</u> Parenteral vaccine injection can be pathogenic for humans (so given i.d. or I.m.)

- FRA test will be +ve in animal at any stage of ds
- Though serum antibodies appear 7 days after vaccination it takes approx 30 days to achieve (immunity lasts for 6 months)
- Anti-rabies serum: prevents replication of virus at the site of bite. Recommended dose of ARS is 40 i.u. i/m

c Course

Pre exposure : 0, 7, 28 HDCV 1ml i.m.

Post exposure: 0, 3, 7, 14, 28 booster on day 90 (if previously vaccinated give only Initial 3 doses i.e. 0, 3, 7).

Intradermal schedule : 80-40-11

PLAGUE

- Plague bacilli can produce exotoxin, endotoxin & fraction-1. These are responsible for virulence.
- In India *tartara Indica* is the main reservoir (not the domestic rat *rattus rattus*) & *X. cheopis* is main vector
- All age & both sex are susceptible
- Flea index** should drop down to zero within 48 hrs of insecticidal spray (carbaryl 2% or malathion). If *X. cheopis* index is more than 1 (≥ 2) → it is indicative of plague outbreak
- A infected area is declared free of plague- if twice the i.p. (12 days) has elapsed since death of last case or 3 months (for wild rodent or 1 month for domestic rodent) has elapsed since last sign of plague in rodent
- Plague season Sept. - May (because of rodent factor) in north India.
- DOC for chemoprophylaxis (in contacts of a pt of pneumonic plague) is tetracycline & for T/t is streptomycin

c Stages of plague

Point	Bubonic	Pneumonic	Septicemic
IP	2-7 days	1-3 days	2-7 days
CI/F	Suppuration is favorable sign	Highly infectious via droplets	
Remark	M/c type	Man man spread +nt	

- Typhoid is regarded as -- Index of general sanitation of country.
- Tuberculosis is called -- Barometer of Social Welfare.
- The Captain of all the men of death.
- White plague
- Black death term was used for --- Plague.
- Cholera was termed as --- Father of public health.

TYPHOID (Enteric fever)

- Man is the only known reservoir
- Age group 5-19 yr. But can affect younger children.
- T~ is regarded as **index of general sanitation** of country.
- Carrier rate is 3% (a person who excrete bacilli for > 1yr after clinical attack is called chronic carrier). *Chronic carriers are present in GB.*
- Carriers are m/c source of infection in typhoid. There are 3 types of carriers
Convalescent carriers - Patient who continue to shed bacilli in feces for 3 wks - 3 months after clinical cure.
Temporary carrier - Who shed bacilli 3 months - 1 year.
- Bacilli usually persist in the GB and kidney and carriers are excreted in feces (fecal carrier) or urine (urinary carrier)
- Fecal carriers are more frequent > than urinary**
- Cases M>F but carrier state F>M (and in older age group, > 40 yr.)
- Urinary carriers are more dangerous than intestinal (Fecal) carriers**
- There is no evidence that typhoid bacilli are excreted in sputum / urine
 (Carriers may be excreted in urine)
- Ulceration of Peyer's patches in gut is common in 3rd week.
- Enteric shock is common in 3rd - 4th week of fever.
- DOC for carriers of typhoid --- Ampicillin.

- c Order of seroconversion —
BASU (Blood culture is best in 1st week, Agglutination or Widal is useful in 2nd week, stool and urine tests c/b employed in 3rd and 4th week of fever)
- c Blood culture is diagnostic and most specific.
- c Typhidot IgM and IgG test is a quick testing method based on antibodies detection.
- *Typhoid fever is best diagnosed by blood culture.*
- *Cholecystectomy and commitment ampicillin + probenecid therapy has been regarded most successful approach for eradication of carriers.*
- *Carriers are diagnosed by culture of bile (obtained by duodenal aspirate)*

CHOLERA

- c Mass chemoprophylaxis is not advised for the total community in case of cholera epidemic
- c In case of epidemic first to do..... verification of diagnosis
- c Cholera is a notifiable disease locally, nationally and internationally
- c Tetracycline is the DOC for chemoprophylaxis
- c Tetracycline is equally effective in children
- c Antibiotics in t/t:
Doxycycline is the DOC for adults, since a single dose suffice.
- Furazolidone is the antibiotic of choice for pregnant women**
- TMP-SMX (cotrimoxazole) is the antibiotic of choice for children.

KALAZAR

- c Napier's aldehyde test is used for d/g.
- c **Endemic in children from Bihar.**
- c Fever + hepatosplenomegaly + hyperpigmentation.

FILARIA

- c Man is definitive host & mosquitoes are intermediate host
- c **In filarial disease (obstructive stage) Mf are not found in blood**
- c Vector for *W. bancrofti*: - *Culex fatigans*
B. malayi & *B. timori* :- *Mansonia*, *anopheles*
- c *Occult / cryptic filariasis* -- classical Clf of *F~* are absent & *Mf* are absent in blood. *TPE* seen
- c Membrane filter concentration method (MFC): most sensitive method for detecting low density microfilaremia.

- c **Clinical parameters for incidence** are adeno-lymphangitis, epididymo-orchitis (acute symptoms) **for prevalence**- lymphedema, elephantiasis, hydrocele, chyluria
- c **Filaria endemicity rate** : $Mf \text{ rate} \pm \text{disease rate}$
- c **Average infestation rate** : indicates prevalence of *Mf* in population (in 20 cu. mm)
- c Bancroftian type is not a zoonosis (*B. malayi* & *T. perstans* are exception).
- c *F~* is endemic all over India except north & East regions (J&K, Delhi, Punjab, Haryana, H.P., Chandigarh, Rajasthan, Nagaland, Manipur, Tripura, Meghalaya, Sikkim, Arunachal Pradesh, Mizoram, Dadra).
- c *Beuteu index* is a larval index for *Aedes aegypti* (No of +ve cases containing larva $\times 100$ / home inspected) .
- c *Mf* of *W. bancrofti* sheathed, active in peripheral blood at night (10:00 pm to 9:00 am).
- c DOC : DEC (72 mg/kg)

Onchocerciasis:

It differs from other filaria in that

- there is no diurnal periodicity, no sheath, Adults are present in s/c tissue & *Mf* are present in skin and eyes.
- Vector is *Simulium* (blackflies) & causes, snowflake corneal opacities (river blindness)
- DOC : *Ivermectin*

JE

- c It is a Zoonosis affects mainly animals, incidentally to man. **man is incidental dead end host.** (man to man transmission does not occur), Subclinical infection is seen. Horses show symptoms
- c Caused by group B arboviruses (flavivirus)
- c *Culex tritaeniorhynchus* (or *C. Vishnuvi*) is the main vector.
- c Rice field is breeding place (zoophilic)
- c Pigs act as amplifier host.
- c Case fatality rate -20 - 40 % (average 30%)
- c Re-vaccination required after 3 yrs.
- c Death occurs in about 9 days (3×3)
- c Vaccination required for children < 3 yrs.
- c Spraying up to 3 km range
- c Immunity develops in 30 days, persist for 3 yrs

[remember with funda of 3]

- Among arboviral d/s *chikangunya* is caused by alpha virus other d/s are usually caused by flaviviruses.
- JE, KFD, Dengue, YF all are caused by flaviviruses.
- *Guneworm infestation* is common in workers of stepwell.

YELOOW FEVER

- Exzootie in India.
- Aedes aegypti is the main vector.
- Aedes aegypti index is kept $\leq 1\%$ at sea ports & in towns for irradiation of YF (Endemic control).
- 400 m belt is kept free of vector breeding.

DENGUE

- Reservoir of infection are both man and mosquito. All ages and both sex are susceptible
- Aedes aegypti is the main vector
- DHF is caused by ---Re-infection with different serotypes of dengue virus
- I.p. is usually 5-6 d
- Usually malnourished children are protected, while well nourished children are affected
- India is in category B, where DHF is an emerging disease, cyclical epidemics are becoming more frequent
- Transovarian transmission is seen with dengue virus
- A clinical d/g of dengue derives from high index of suspicion and geographic distribution.
- Grading of severity of Dengue infection**

Grade	Cl/f	Lab/f
DF	Fever + ≥ 2 of these signs headache, retroorbital pain, myalgia, arthralgia	Leukopenia, Thrombocytopenia \pm No evidence of plasma loss
DHF I	Above + positive Hess/ torniquet test	Thrombocytopenia < 1 lakh /mm ³ ; Hct $\geq 20\%$
DHF II	Above signs + spontaneous bleeding	"
DHF III	Above signs + circulatory failure	"
DHF IV	Above + profound shock (undetectable BP and periph. pulses)	"

- DSS includes DHFIII and DHF IV.
- Transovarian transmission is seen with dengue virus.
- The most sensitive test for d/g is IgM-capture enzyme-linked immunoabsorbent assay (ELISA).
- Interpretation of dengue serology

IgM	IgG	Interpretation
-	-	Too early sample or no DF
+	-	Early stage of primary DF
+	+	Recent or ongoing primary DF
-	+	Past dengue infection
+/-	+++	Secondary dengue infection (Reinfection)

Severe Acute Respiratory Syndrome (SARS)

- Earlier contacts were detected in Toronto & Hong Kong
- Agent is SARS associated corona virus.
- Mean incubation period is --- **2-7 days**
- Lab/f: Lymphopenia, \uparrow LDH and CPK, thrombocytopenia
CXR : w/l or b/l peripheral lung infiltrates
- All specimens to be sent under cold chain condition (2-8°C) within 24 hours to the specified labs.
- T/t** : O_2 + antibiotics for community acquired pneumonia (e.g. cefotaxime/clarithro). Neuraminidase inhibitor such as Oseltamivir for T/t of influenza A & B
Oral/ IV Ribavirin \pm corticosteroids are also given
- CFR is 13.2% for <60 yr while 43% for >60 yrs.
- Confirmatory centres in India :--- National Institute of Virology, Pune, and NICD, New Delhi.

SWINE FLU (H1N1 Disease)

- Respiratory infection caused by **influenza A virus (H1N1)**. H1N1 is a genetic re-assortment of four viruses i.e. 2 swine + 1 human + 1 avian virus
- Worldwide pandemic is running in the year 2009
- Contagious d/s. Person to person spread is known to occur through coughing, sneezing etc. The period of infectivity is 1 day prior to symptoms to 7 days post-onset. Children are contagious for longer period (upto 10 days) and have more severe infection
- High risk groups : Children < 5yrs, immunocompromised, pregnant females, asthmatics, etc.
- Symptoms : Headache, fever, coryza, cough, nausea, etc.
- CXR is s/o B/L pneumonia with pulmonary edema.
- D/g** : Based on detection of virus.
 - Commonly used method of virus detection is--- **RT-PCR** of **pharyngeal/throat swab** (or virus culture in some centres), which is collected at the time of peak infectivity (4-5 days of onset of symptoms)
- Prophylaxis** : **N-95 or higher face mask** are recommended to provide barrier to transmission
- T/t** : Neuraminidase inhibitors **Temiflu (oseltamivir)** is DOC. Relenza (Zanamivir) is also useful
- Vaccines are available ---
 - Surface antigen based vaccine contains Influenza A H1N1 + H3N2 + Influenza B e.g. Influvac
 - Split virion based vaccine also contains Influenza A H1N1 + H3N2 + Influenza B e.g. Fluarix
 - Nasal vaccine

TETANUS

- Toxin is TETANOSPASMIN which blocks presynaptic neurotransmitter release in CNS. Toxin acts on motor end plate of muscles, brain, spinal cord and sympathetic NS (but **not** on parasympathetic system)
- **Trismus (lockjaw)** d/to masseter spasm) is the first sign.
- Incubation period is usually 7-10 days. (Shorter the incubation period, worse the prognosis)
- Latent tetanus: Wound is healed and it appears after a long incubation period. It carries better prognosis.
- Different postures seen in tetanus :
Opisthotonus: backward bend d/to spasm of back m/s.
Emprosthotonus: Forward bend d/to spasm of front m/s.
Pleurothotonus: Lateral bend.
- Risus sardonicus: Smiling facies, due to spasm of zygomaticus major.
- Cephalic tetanus: facial muscle first involved (due to 3, 4, 6, 7 CN affected), follow head injury/ear infection.
- Urinary retention, DTR exaggerated
- Mentation (intelligence) is unimpaired

MALARIA

Indicators in Malaria

Indicator	Significance
ABER	Index of <u>operational efficiency</u>
API	Malaria <u>surveillance parameter</u> (based on both active & passive surveillance) gives <u>incidence</u> in community. ABER is required to calculate API
HBI (Human blood index)	Freshly fed female anophelines whose stomach contain human blood. <u>Indicates degree of anthrophillism</u>
Inoculation rate	Man-biting rate \times sporozoite rate
IPR (Infant parasite rate)	Most sensitive <u>index of malaria transmission</u> in community / endemic area. Most important index in endemic area (endemicity of d/s)

- **Relapse :**
Reappearance of parasitemia following adequate blood schizonticidal therapy. In malaria **relapses** are d/ to hypnozoites (or original sporozoite induced, liver schizonts). Seen in **P. vivax** and **P. ovale**.
In Pf and Pm infections latent liver schizonts do not occur, so relapses are usually not seen.

• Reservoir :

A human **reservoir** is one who harbors the sexual forms (gametocytes) of parasite.

• Recrudescence :

Secondary waves of parasitemia d/ to survival of erythrocytic stage at low level for prolonged time. It occurs in **P. falciparum** (for the year) and in **P. malarie** (for up to 30 years).

• Schizogony :

Asexual reproduction during which nucleus undergoes division.

→ Infectious stage is sporozoite which is transmitted to the host by bite of female anopheles mosquito

→ Relapse is not seen in transfusion associated malaria.

→ Persons with Duffy -ve blood group are protected against vivax malaria

→ Persons with sickle cell ds, thalassemia and G-6-PD deficiency are relatively resistant to falciparum malaria.

→ Durck granuloma is seen in cerebral malaria.

→ Thick smears are used to identify malarial parasite & thin smear for identification of species.

Operational Guidelines for Malaria

- National Drug policy (2007) on malaria gives emphasis on complete t/t in diagnosed cases rather than presumptive t/t only.
- Primaquine for 15 days in place of 5 days.
- RDT kits are supplied in far or tribal areas.
- T/t of uncomplicated chloroquine resistant (or MDR) falciparum malaria : Artesunate 100 mg BD x 3 days.

Treatment Guidelines for Malaria

- Non-pregnant adult and pediatric patients **P. falciparum** infections acquired in areas with chloroquine resistance : atovaquoneproguanil (Malarone) or artemether-lumefantrine (Coartem). These are fixed dose combination medicines.
- For pregnant women diagnosed with uncomplicated malaria caused by **P. malariae**, **P. vivax**, **P. ovale**, or chloroquine-sensitive **P. falciparum** infection, prompt t/t with chloroquine /hydroxychloroquine may be given. For chloroquine-resistant **P. falciparum** infection, prompt treatment with either mefloquine or a combination of quinine sulfate and clindamycin is recommended.

	P. falciparum	P. vivax	P. ovale	P. malariae
◦ Average I.P. (intrinsic)	12 d	14	17	28
◦ Erythrocytic cycle	48 hrs	48	50	72
◦ Intrahepatic phase (pre-eryth schizogony)	5.5 d	8	9	15
◦ RBC preference	Younger cells (but can infect RBCs of all stages) (Heavy parasitemia)	Only reticulocytes	Reticulocytes	Old cells (prolonged parasitemia)
◦ Exoerythrocytic cycle (latent liver schizonts)	-	+	+	-
◦ Relapse	-	+	+	-
◦ Recrudescence	+	-	-	+
	(For few years)			(for many /up to 30 years)
◦ Pyrogenic density	10000 parasites/ μ l	100 para/ μ l		
◦ Merozoites/hepatocyte	40,000 maximum	10,000	15,000	12,000
◦ Type of fever	malignant tertian (aperiodic quotidian)	benign tertian	Ovale tertian	Quartan (fever every 4th d)
◦ Morphology	◦ Only ring forms ◦ Crescents+, banana shaped gametocyte ◦ Schizont -nt ◦ Mature trophozoite ^{nt} ◦ Accole forms+ ◦ Multiple infection of RBC ⁺	◦ Enlarged RBC ◦ Large rings/tropho ⁺ ◦ Largest schizont (12-24 merozoite)	◦ slightly enlarge RBC ◦ schizonts ⁺ ◦ RBCs pear shaped fimbriated & crescentic	Bands/rectangular forms Small RBC
◦ Pigment & dots	◦ Black (Maurer's) [Maurer's dots]	◦ Yellow, brown [Schüffner's]	Dark brown [James dots]	[Ziemann's dots]
◦ Clinically	◦ Causes cerebral / Severe malaria (malignant malaria)	◦ may cause splenic rupture		May cause nephrotic synd.

→ Black water fever is a c/c of falciparum malaria.

TUBERCULOSIS

- Mass miniature radiography was the mainstay of diagnosing TB before 1989.
- Only 2 sputum examination are recommended now a days.

DOTS

- Under RNTCP all patients are provided short -course chemotherapy free of cost.
During the intensive phase of chemotherapy all the drugs are administered under direct supervision called 'Direct observed therapy short term' (DOTS).
- DOTS is given by peripheral health worker (eg. MPW) k/ as DOT agent.
- It ensures high cure rates, compliance.

RNTCP

- The GOI, WHO & world bank together reviewed the NTP in year 1992.
- Revised strategy was introduced in the country as a Pilot project since 1993 in a phased manner as pilot phase I, II & III.
- Strategy are
 - Achievement of least 85% cure rates of infections cases through supervised short course chemotherapy (DOTS)
 - Case finding is based on quality **sputum microscopy** to detect at least 70% of case
 - Involvement of NGOs.
- Microscopy centres are established in RNTCP districts for every one lakh population. They are located in the CHC, PHC, Taluka hospital or in the TB dispensary.

- Combination of > 2 drugs in TB- used to prevent drug resistance, it may increase toxicity (cumulative effect)
- Primary resistance (pretreatment resistance) is d/to episomes.
- Secondary resistance (Acquired) – emergence of resistance after ATT.
- WHO defines a multidrug resistance (MDR) strains 'one that is at least resistant to INH & RMP'.
- Primary dg resistance in India is mostly to INH (20%) followed by streptomycin (10%) & RMP (1%)

c Rifampicin is most potent anti-TB drug

XDR-TB

XDR Strains are extensive drug resistant (XDR) strains of mycobacterium tuberculosis that are also resistant (apart from first line drugs) to at least the fluoroquinolones and one or more of the injectable drugs like amikacin, kanamycin or capreomycin.

XDR - TB have poor t/t options and poor prognosis.

Epidemiological parameters in tuberculosis

Parameters	Definition	Current level in India
- Prevalence of infection	% of MT + ve	30.4%
- Prevalence of d/s (TB) (case rate)	% of sputum+ve case, Best available practical index to estimate case load or no. of infectious cases in community	4 per 1000
- Prevalence of "suspects"	Based on CXR	No significance
- Incidence of infection (Annual infection rate)	Newly infected population (new MT converter)	168 lakh (1.7%)
- Tuberculin conversion index	Best indicator for evaluation of TB problem and its trend	0.6-2.3%
- Incidence of new cases	Is the % of new cases (confirmed by bacterial examination)	1.5 per 1000

- In developing countries every 1% of annual risk of infection corresponds 50 new cases for 1 lakh general population

LEPROSY

o Bacterial Index (BI)

BI is the only objective way of monitoring the benefits of t/t in leprosy. WHO grading of smears of BI is

- (-) No. bacilli found in any of the 100 oil immersion fields (OIF)
- (+) ≤ 1 bacillus in each microscopic or 1-10 average bacilli in 100 OIF
- (++) 1-10 average bacilli in 10 OIF
- (+++) 1-10 bacilli in each fields

[G is added if globi are +nt]

- o BI in paucibacillary leprosy is <2 & in multibacillary > 2
- o Dharmendra's scale & Ridley's logarithmic scales are also used for reporting BI.
- o BCG have no cross reactivity with lepromin.
- o **Lepromin Test** is useful in evaluation of CMI (immune status) of leprosy patient and to classify leprosy. It also estimates prognosis.
- o **Histamine Test** - is for early detection of nerve damage.
- o **Morphological Index (MI)** - % of solid staining bacilli in smear.
- o *Operational Indicators of leprosy control activities*
 - Relapse rate, case detection ratio etc
- o **Relapse rate** is one of the best indicator of efficacy of drug regimen.
- o *Epidemiological indicators are*
 - **Incidence rate** --- Most sensitive index of leprosy transmission. It measures effectiveness of action taken (reduction of transmission)
 - **Prevalence** - Provides a measure of the "case load" and useful in the planning of the t/t.

HIV / AIDS

- o In India AIDS is m/c caused by **HIV-1 subtype C**.
- o HIV-1 is also more common than HIV-2 worldwide
- o M/c mode of transmission is sexual transmission
- o AIDS was first recognized in India in Chennai in 1986.
- o HIV virus was first isolated in 1983 in patient suffering from pneumocystis carinii and by 1984 it was demonstrated to be the causative agent of AIDS.
- o National AIDS Control Program (NACP) was launched in year 1987.
- o Six high prevalence State of India are – Tamil Nadu A.P., Maharashtra, Karnataka, Manipur, Nagaland and Delhi.
- o On 1st Dec. 2003, WHO and UNAIDS announced a detailed plan to reach the "3 by 5 target" of providing antiretroviral treatment (ART)

- Most prevalent HIV state is Tamil Nadu.
- At present NACP-III is in force. It was launched in 2007-08

- In India, M/c route of infection is sexual.
- Efficacy of transmission is maximum with blood transfusion.
- Predominant opportunistic infection in AIDS patient is TB followed by candidiasis.

Rheumatic Fever/ RHD

- RF occurs in 1-3 % of streptococcal infections.
- Caused by group A beta hemolytic streptococci.
- Primary prevention** : All significant sore throats in school aged children must be suspected to be rheumatic. T/t initiated within 1 wk of streptococcal infection is likely to prevent RF. A single i.m. dose of Benzathine benzyl penicillin 1.2 million (in adults) or 60,000 units (in children) is recommended.
- Secondary prevention** :
For children who already had RF Use *injection benzathine penicillin benzyl 1.2 million (12 lakh) units i.m. every 3 weekly* Now a days preferred t/t is oral penicillin V 250 mg BD or i.m. procaine penicillin G
Secondary prophylaxis should be continued till ---
18 years or 5 yrs after initial attack whichever comes later (for rheumatic arthritis)
25 years of age or 10 yrs after initial attack whichever is longer (for rheumatic carditis)
Life long prophylaxis (for established valvular lesions)
- M/c cardiac lesion in children is MS and in adults is MR.
- Best indicator of RF control programme --- prevalence of RHD in 6-14 yrs school children.

Obesity

- WHR (waist :Hip ratio)** is an approximate index of abdominal fat mass & total body fat. Over the past 10 years or so, it has become accepted that high WHR (> 1.0 in men & > 0.85 in women) indicates abdominal fat accumulation.

Other indicators of obesity

- Broca's index** = $Ht (cm) - 100$
- Corpulence index** = Actual weight/desirable weight should be < 1.2
(Does not include height)

- Quetelet's index (BMI)** = $Wt (kg)/ht^2(m)$
- Skinfold thickness(SFT)** = Most accessible method & most used method for subcutaneous fat.

- Ponderal Index(PI)** = $\frac{Ht (cm)}{\sqrt[3]{Body\ wt\ in\ Kg}}$

- Ponderal Index for child** = $Wt\ in\ gm / (Ht\ in\ cm)^3$

- BMI for Asians**

10 - 18.5	18.5 - 24.9	25 - 29.9	30 - 39.9	>40
Under weight	Healthy	Over weight	Obese	Morbid obesity

- BMI of normal Asian males 18.5 - 24.9
- Bariatric surgery is an emerging field in obesity t/t

Important risk factors for development of DM, HTN and CHD coronary/ ischemic heart diseases (CHD)

Risk factors	HTN	CHD	DM
Non modifiable			
Age & sex	++		
Family history	+	+	+
Personality		Type A personality	
Modifiable			
Obesity	+	+	+
Salt intake	+	-	-
Saturated fat, hypercholesterolemia	+	+	+
Dietary fibers	↓	+	↓
Smoking	+	+	
Alcohol	+	+	+
Physical inactivity/ sedentary habits	+	+	+
Stress	+	+	+
Others	OCPs (estrogen component)	DM, HTN, OCPs	PEM in infancy

- Smoking have no relation with diabetes
- Smokers are protected against (less incidence of) ulcerative colitis, parkinsonism, sarcoidosis.
- Vit A is protective against lung cancer
- Male gender and increasing age are the two most important risk factor for development of IHD.
- Heart disease (CADs) are on ↑ing trend in India compared to West.

SOCIAL HEALTH

- **Social mobility:**
Movement of individuals, families, or a group from one social position to another (across socioeconomic level)
- **Socialization :**
Process by which culture, principles, knowledge, & thought process is transmitted from one generation to the next.
- **Social medicine :**
Study of a man as a social being in his total environment
- **Socialized medicine:**
Medical services & education provided by state but regulated by professional groups
- **Social Science:**
Discipline concerned with scientific examination of human behaviour.
Social Science include : Economics, Political Science, Sociology, Social psychology & anthropology out of which last 3 (SAS) constitute Behavioural sciences.
- *Behaviour Science include :* Sociology, Social psychology & anthropology.
- **Socioeconomic status scales :**
BG Prasad Scale — Used in both rural and urban areas
Pareek's Scale — Used in rural India
Kuppuswamy Scale — Used in urban India
- Community participation is maximum in planning of intervention.
- Indian society is a close class system.
- *Emporiatrics deals with the health of travellers.*
- *Eugenics is the science which aims at improving the genetic constitution of human population.*
- *Ergonomics is the science of fitting workplace conditions and job demands to the capabilities of the working population.*

- Calorie requirement in urban area is 2400 Kcal/d & in rural area is 2600 kcal/d.
- **Wealth Index :** Is an indicator of the level of wealth that is consistent with expenditure and income measures. It is one of the background characteristics used in the NFHS-III as an index of economic status.

Child placement in social agencies:

- **Orphanages** : No home
- **Foster homes** : Rearing child away from home with structural facilities.
- **Brostals** : Boys >16 yrs who are misbehaved are kept in brostals.
- **Remand homes** : Child is placed under care of doctor, psychiatrist & other trained person.

HEALTH EDUCATION

- Socratic method of teaching or two way communications are
 1. Focus group discussion
 2. Panel discussion
 3. Symposium
- Didactic methods of teaching or one way communication
 1. Lecture method
 2. TV
 3. Radio
- **Delphi method**
Is a systematic, interactive forecasting method which relies on a panel of independent experts.

DEMOGRAPHY AND MCH CARE

AGR

- Annual growth rate $AGR = CBR - CDR$
- Growth is said to be very rapid when AGR is 1.5-2 & explosive when > 2.
- AGR of India (2001) was 1.93 (very rapid growth rate) .
- **Population doubling time :No. of years taken to double population = $70 / AGR$** e.g. growth rate of India is 2.1 % it will take < 35 yr to double its population.

AGR	Growth	PDT
0-0.5	Slow	
0.5-1.0	Moderate	
1.0-1.5	Rapid	50-70 yrs
1.5-2	Very Rapid	
>2	Explosive	<35 yrs

Stages of demographic cycle

Stage	Characteristic	Examples
1. High stationary	High BR, High CDR (Population remains stationary)	India before 1920
2. Early expanding	High BR, CDR ↓ing	South asian & African countries
3. Late expanding	↓ing BR, ↓↓ DR (AGR high becoz birth >> deaths)	China, Singapore, India
4. Low stationary	Low BR, Low CDR (zero population growth)	
5. Declining	BR < CDR	Germany, Hungary

Population composition in India

- School age children constitute 25% of Indian population. Although India occupies only 2.2% of the world's land area, it supports over 15% of the world's population. Almost 35% of Indians are <15 years of age.
- Uttar Pradesh is the most populous state and Dadra and Nagar Haveli is the least populated state in India.
- Age group 0-4 5-14 15-59 60+
 11% 22% 59% 7%
- India's age pyramid mainly constitutes children & population of pre-reproductive age.
[Broad base & tapering top]
Acc/ to 1991 census children < 15 yr 40% (0-4=12.8%, 5-9=13.2% & 10-14= 11.7%)
- Women of child bearing age constitute 19%.
- Total population 121.01 Crores in 2011

Vital Statistics

Parameter	2001	2011	Remark
Population density	325	382	
Sex ratio (F:M)	933	914	Best reported in Chhattisgarh (1018) worst in Haryana (836)
Urban population %	28	31%	
Life expectancy at birth	61.8 (M) 63.5 (F)	62.6 (M) 64.2 (F)	
AGR		1.64%	
CBR	25.4	21.8	
CDR	8.4	7.1	
MMR (per lac LB)	301	212	
IMR	66	44	
CMR (Child 0-4 MR)	19.3	14.1	
USMR		55	
TFR	3.1	2.4	

- Literacy rate - total 65.38 (M=76, F=54)
- Sex ratio is 940 F/1000M (Juvenile sex ratio or child sex ratio). Internationally the sex ratio is considered no. of males per 1000 females.
- Annual GR = 1.64 % (2011)
GR = 17.64% (highest of Dadra & Nagar Haveli 55.5% and lowest of Nagaland - 0.47%)
- National family health survey-2 (NFHS-2) was conducted in India during 1998-99.
- According to NFHS-3 % of institutional deliveries are 40.4%.
- National socio-demographic goals for 2010 are ---to achieve 100% registration of births, deaths, marriages & pregnancy, 80% institutional deliveries & 100% of them by TBA.

Some fertility related indicator

- **Abortion rate**

$$= \frac{\text{No. of abortions}}{\text{No. of women of child bearing age}} \times 1000$$

- **Abortion ratio**

$$= \frac{\text{No. of abortions in unit time}}{\text{No. of live births in the same time}} \times 1000$$

- **Marriage rate (crude)**

$$= \frac{\text{No. of marriage in a year}}{\text{Mid year population}} \times 1000$$

General Marriage rate

$$= \frac{\text{No. of marriage in 1 year}}{\text{No. of unmarried persons in 15-49 yr gp}} \times 1000$$

Child woman ratio

$$= \frac{\text{No. of child 0-4 year}}{\text{Per 1000 women of child bearing age}} \times 1000$$

Causes of infant mortality (<12 months)

Neonatal mortality (0-28 d)		Post neonatal mortality (28 d - 12 months)
Early NNM (0-7 d)	Late NNM (7-28 d)	ARI
◦ Prematurity	◦ Sepsis	◦ Diarrhoea
◦ LBW	◦ Tetanus	◦ Malnutrition
◦ Birth asphyxia (endogenous factors)	(endo/exogenous factors)	(exogenous factors - environmental & social) -ve

Denominator is total no. of live birth.

[Remember that in an equation /formula numerator is the value above the line and denominator is the value down (below) the line]

◦ **PMR (Perinatal MR)** : numerator is still birth + early neonatal deaths.

◦ **MMR (Maternal MR)** :

MMR is a ratio in which maternal deaths are expressed as per 1 lakh live births. Numerator include all maternal deaths related to pregnancy + delivery + upto 42 days post delivery while denominator is **total no. of live births** in the same area in same yr.

→ **RHIME** is a new method of MMR estimation (a form of verbal autopsy)

→ Neonatal mortality is higher for males than for females (but IMR is higher in females)

→ Neonatal deaths are maximum in first month of life out of which maximum in first seven days & out of these seven days first hour is the most critical period of neonatal life.

→ Neonatal mortality is major contributor of infant mortality (70%)

→ Tetanus is an important cause of late neonatal mortality

→ Neonatal mortality rate of India is 45 per 1000 live births (49 in rural areas and 28 in urban areas)

→ Congenital anomalies are rare cause of NNM

→ M/c cause of infant mortality in India --- **LBW** (51%) > **ARI** (17%)

→ M/c cause of child mortality (under five) in India --- **Neonatal causes** (37%) > **ARI** (19%) > **Diarrhoeal d/s** (17%)

→ Child death rate (1-4 year mortality rate) is a more refined indicator of the social situation in a country than **IMR**. Major causes in this age group are diarrhoeal diseases and **ARI**

Indicators of fertility

◦ **BR** : Simplest indicator of fertility

◦ **GFR** :

No. of live birth/mid yr population of females (15-49 yr).

◦ **GMFR** : Married & fertile women are denominator

◦ **ASFR** : Sensitive Indicator of FP achievements

◦ **ASMFR** : Most refined

◦ **CDR**

No. of death/ mid year population. It is an indicator that shows relationship b/w population and age specific mortality.

◦ **TFR**

Gives approximate magnitude of **completed family size** (TFR of India is 3.2)

◦ **GRR**

Average no. of girls that would be born to a woman if she experiences current fertility and *no mortality*.

◦ **NRR**

Average number of a girl child (daughter) that a new born girl will bear during her lifetime assuming fixed age-specific FR & ASMR. It is a **demographic** indicator

To achieve NRR of 1 or 2 children norm CPR should be >60% (had to be achieved by 2006)

◦ **Couple Protection Rate (CPR)**

CPR was 31% in 1987. 50-60% of births per year in India are birth order ≥ 3 .

→ To achieve NRR of 1 or 2 children norm CPR should be >60%

→ No. of condoms needed for protection of a couple for one year --- 72

◦ **Eligible couples** is a currently married couple with wife in reproductive age group (15-45 yrs). In India eligible couples are 150-180/1000 population. 20% eligible couples are in the age group 20-24 years.

Case fatality rate, prevalence, proportional mortality rate, SMR & pregnancy rate all are ratio

PQLI Indicator (Physical Quality of life Index)

1. IMR
2. Life expectancy at age 1yr
3. Literacy [mnemonic ILL]

PQLI Ranges from 1-100 .In India it is 43.

Human Developmental Index (HDI)

- It includes -
 - Longevity (life expectancy at birth)
 - Income (real GDP per capita or purchasing power in parity dollars)
 - Knowledge / education (adult literacy rate & mean yrs of schooling)
- [mnemonic : Like]
- Composite index of achievements in most basic human capabilities.
- HDI is highest in Kerla. Current value is 0.467

→ *GDI (Gender-related Developmental Index) – given in 1995, reflects achievements in the basic human development adjusted for gender inequalities*

→ *GEM (Gender Empowerment Index) given in 1995, measures gender inequalities in economical and political opportunities.*

→ *Human Poverty Index (HPI) is measurements of deprivation in basic dimensions of HDI.*

→ *For India HDI is 0.619, PQLI is 43 & HSI (Human Suffering Index) is 70.*

→ *Sullivan's Index: Life free of disability*

→ *DALE (Disability Adjustment Life Expectancy) — Measure used to express the global burden of disease.*

→ *HALE (Health Adjustment Life Expectancy) — Based on life expectancy at birth but includes an adjustment for time spent in poor health*

- **DALY (Disability Adjusted Life Years)** --- Indicator which developed for the d/s burden which quantifies in a single indicator, time lost d/to premature death with time lived with a disability. *One DALY is one lost year of healthy life.* Highest DAY is for psychiatric disorders - Schizophrenia, unipolar & bipolar MD.
- **Disability free Life Expectancy** --- Number of years of projected life expectancy that will be spent free of disability.
- **KAP** : KAP stands for Knowledge attitude & Practices. .KAP surveys were applied in HIV and family planning KAP GAP indicates unmet needs of family planning. applied to married women.

- **IEC** :IEC stands for Information, education and communication.
- **Unmet need** :Refers to 15-49 yr old married women who are not using contraception or family planning methods.

RCH Programme

RCH phase I

- Launched on 15th Oct'97 as a result of recommendation suggested by Cairo conference.
- Target free, **decentralized** program aimed at satisfaction of individual (client centered approach). Includes components of child survival + safe mother hood and
 - + **Prevention / management of RTI / STD, AIDS**
 - + **Client approach to health care**
 - + Family planning
- 1st referral units (FRUs) are set up at sub district level
- Targets for various health activities are set up at *district level*
- Districts are divided on basis of female literacy rate + CBR
- Control of RTI/STDs in R~ is likely to benefit in AIDS control program.

RCH phase II

- Launched in april 2005 to reduce maternal & child morbidity with emphasis on rural health care
- 3 strategies :
 1. Essential obs care
 2. Emergency obs care
 3. Strengthening referral system.
- Kit A,B,C are provided for subcentre while kit D is provided for PHC.

IMCI

It is a global programme. It involves integrated approach to manage childhood illness with focus on ----
Diarrhea, ARI, malaria, measles and malnutrition.

IMNCI

- It is Indian version of IMCI. It also includes neonatal period (first 7 days of life)
- Incorporates national guidelines on --- Diarrhea, Measles, Malnutrition, anemia, vitamin A supplementation, and immunization schedule. ARI (Otitis media, upper respiratory infections) is also included.
- Promotion of breast feeding and nutritional counselling is included in IMNCI.

Important Index

- **Pearl Index** is a measure of contraceptive efficacy. It is defined as the number of "failures per 100 women years of exposure" this rate is given by the formula:
Failure rate per HWY
= $\frac{\text{total accidental pregnancies}}{\text{Total months of exposure}} \times 1200$
Life table analysis is a better measure for this.
- **Life table analysis** is the best measure for contraceptive efficacy, a biometer of population. Special type of cohort analysis and is an example of indirect standardisation. Used for mortality, reproductivity (contraceptive failure) and chances of survival.
- **Chandler Index** is average number of hookworm eggs per gram of stool. It is useful in epidemiological studies and assess response to t/t. Index < 200 indicates that hookworm infection is not of much significance and > 300 indicates major public health problem
- **Soiling Index/ smoke index** is an indicator of air pollution. It is based on best indicators of air pollution-3s i.e. sulphur dioxide, smoke, suspended particles

Remember

- **Pearl index** — Measures contraceptive efficacy
- **Chandler's index** — is average numbers of Hookworm eggs / gm of stool
- **Soiling index** — is an indicator of air pollution (smoke index)
- **Bacterial index** — is used for classification of leprosy
- **Wealth index** — is an index of economic status of households based on NFHS-III
- **Beuteu index** — is used for *Aedes aegypti*

Integrated Disease Surveillance Project (IDSP)

Launched in Nov. 2004. It is decentralized, state based surveillance system in the country.

Baby - friendly hospitals initiatives (BFHI)

- Mother & child are left together 24 hrs a day
- Feeding on demand. Promote mother to initiate breast-feeding within first hr of birth in normal delivery & 4 hrs following cesarean section.
- Exclusive BF is recommended till 6 month. No food / water / drink other than breast milk.

NATIONAL HEALTH POLICY 2002

[Goals to be achieved by 2015]

- Eradicate Polio and Yaws --- 2005
- Eliminate Leprosy (2005), Kala-azar (2010), & Lymphatic Filariasis (2015)
- Achieve zero level growth of HIV/AIDS --- 2007
- Reduce mortality by 50% on account of TB, Malaria and other vector & water borne diseases --- 2010
- Reduce prevalence of blindness to <0.3% --- 2010
- Reduce IMR to 30/1000 & MMR to 100/lakh --- 2010
- ↑ utilization of public health facilities from current level of <20% to >75% --- 2010
- Establish an integrated system of surveillance, National Health accounts and Health statistics --- 2005
- ↑ health expenditure by Govt. as a % of GDP from the existing 0.9% to 2.0% --- 2010
- ↑ share of central grants to constitute at least 25% of total health spending --- 2010
- ↑ state sector health spending from 5.5% to 7% of the budget --- 2005

Mch Goals and Current Levels :

NFHS-3	Current 2007-08	National socio demography goals for 2010	10th FYP Goals (2007)	National Health Policy 2000 (by 2010)
FP Indicators				
- CBR	23			21
- TFR	2.8			2.1
- CPR	56			Meet all needs
Mortality Indicators per 1000				
- IMR (2009)	54	< 30	45	<30
- NMR	37	-	-	-
- MMR (per lac)	254	< 100	200	100
Services :				
- Fully immunized infants	64%			100%
- TT to pregnant women	80%			
- Institutional deliveries	60%	80%		80
Prevalence of 30% LBW babies				

- In Millenium developmental goals (MDG) IMR has to be reduced to 2/3rd and MMR has to be reduce to 3/4th of current level.

INDIAN ECONOMY

- According to the world health report 2000 India's health expenditure is 5.2 % of GDP
- Indian (economic) real GDP growth for the year 2003 is 7.5-9%
- Annual per capita income 2006-07 is Rs. 33,131
- Real GDP (2005) \$ 3.78 trillion
- Real GDP growth rate (at PPP) 7.1% (2005)
- GDP per capita \$ 1830
- Population below poverty line is 29% (2012). Criteria for below poverty line (BPL) are
 - Per capita monthly income < 360 Rs for rural area and < 540 for urban area .
 - Per capita kilocalorie consumption < 2100 in urban area and < 2400 in rural area.
- 3 Primary d/s of poverty : AIDS, malaria and TB.
- Unemployment rate 7.32%
- Per capita GNP of India is 450 US \$ parity dollars.
- According to world bank's report 2006 India is the 12th richest country of the world.

3 TIER SYSTEM OF HEALTH CARE DELIVERY

Level of care	Institution	Referral level	Population Catered		Staff
			in plains	in hilly / tribal areas	
3 ^o	Medical colleges, Teaching institutions, Apex/ super speciality hospitals	2nd	-	-	
2 ^o	Distt health centres/ Subdivisional hospitals, CHC	1st	1 in 1 lakh	1 in 80,000	
1 ^o	PHC		30,000	20,000	
	Subcentre		5000	3000	MHW, FHW, VW
	Village health posts		1 per 1000	1 per 1000	TBA/dai, AWW, VHGs

[MHW = Male Health Worker, FHW = Female Health worker, TBA = Traditional Birth attendant; VHGs = Village Health Guide]

- Primary health care (essential health care) is the first level of contact of individual/ family
- A Village health guide (VHG) caters a population of 1000. VHG & AWW are working under ICDS scheme.
- Gross root workers (Healthcare personnel at village level) include — AWW, TBA, VHG, and ASHA
- Mini AW centres exist at population of 150-170 in tribal and in accessible areas .
- MHW is MPW male . FHW is MPW female better called ANM (Auxillary nurse midwife)
- Principles of primary health care are — ECAI
Equality, Community participation, Appropriate technology, Intersectoral co-ordination.
- Suggested norms for Doctor to population is 1 per 3,500.
- Ideal bed space in an hospital — 12 feet.

ENVIRONMENT

O₂-Pond

- Also k/as Redox Pond / water Stabilization Pond
- Space required is 22 acre, 1 - 1.5 m deep
- Established method of sewage disposal in small community
- O₂ comes mainly from algae
- Cloudy weather ↓ efficiency of process

Environmental Measures

Apparatus	Used for
1. Pattern Kopfer test	Snow blindness
2. Anemometer	Recording low air velocities
3. Kata thermometer	Very slight air currents (<10 ft/min), cooling power of air
4. Assman's psychrometer	Humidity
5. Symon's raingauze	Precipitation (rain, snow,dew, frost)

- Acceptable level of thermal comfort is : 25 ° -27 ° C CET.
- BOD (Biological oxygen demand) is indicator of organic contents of sewage. BOD >300 indicates strong sewage.

- Day light factor for kitchen should be $\geq 10\%$ & for living room is 8%.
- Air quality in India is controlled by central pollution control board (Ministry of environments and forests).

Contamination of Water : Bacteriological Indicators

- Presence of coliforms (*E. coli*/ *klebsiella*)** : Used for presumptive or most reliable and primary indicator of fecal pollution of water.
- Presence of fecal streptococci** : Indicates recent contamination of water.
- CI. perfringens** : Indicates remote (past) fecal pollution of water.

→ Saline, nitrite, ammonia indicate recent pollution of water

→ Nitrates indicate old contamination.

→ Ideally no coliforms should be present in any sample but for large urban supply, if > 95% of samples are coliform free for consecutive 12 months, it is acceptable.

Drinking water Acceptability Parameters

Constituent	Maximum acceptable level	Standard prescribed levels
Chlorides	600 mg/L or 60 mg%	200 mg/L or 20 mg%
Ammonia	1.5	0.2 mg/L in surface water
pH	6.5 - 8.5	4.4
TDS	1000 mg/L or 100 mg%	< 60 mg%
Iron	0.3 mg/L	

Chlorination

- The principle is to ensure a free residual chlorine of 0.5 mg/L at the end of 1 hr contact period.
- For household purpose "Rolling Boil" for 5-10 minutes is satisfactory. No residual protection offered.
- Chlorine acts best as a disinfectant when pH of water is 7. Turbidity impedes efficient chlorination.
- Disinfecting action of Cl_2 is mainly d/to HOCl (hypochlorous acid)
- Apparatus
 - Chlorine demand of water is estimated by --- Horrocks apparatus
 - Chlorine dose is regulated by / Cl_2 mixing is done by --- Chlorinator
 - Residual level of chlorine is measured by --- Chloroscope

- Break point chlorination**: The point at which the residual chlorine appears and when all combined chlorines have been disappeared is the breakpoint and corresponding dosage is breakpoint dosage.

- Superchlorination** followed by dechlorination done for heavily polluted water whose quality fluctuates greatly.
- Water source should be ≥ 15 m (50 feet) away from latrine.

- The vital layer (*Zoogleal layer*) is the heart of slow sand filter. Also k/as *Schmutzdecke* or biological layer. It removes organic matter of water.

- Chlorine compounds

- Bleaching powder (CaOCl_2)

-- Contains 33% of available Cl_2 if freshly prepared
(Most effective and cheapest way of disinfecting well)

- Chlorine tabs

-- A single tab of 0.5 g is sufficient to disinfect 20 L of water.
(Easy and cheap method to disinfect household water)

- Chlorine gas

-- First choice for disinfection of large body of water.

- Perchloron

-- Also k/as High test hypochlorite (HTH), provides 60-70% available Cl_2

- Tests

- OT- test (Ortho -Tolidine test):

Provides :

within 10 seconds : free Cl_2

after 10-20 min hold: both free and combined chlorine in water with speed and accuracy.

- OTA test (Ortho -Tolidine- Arsenite test) :

Determines free and combined chlorine separately.

→ Iodine is used for emergency disinfection of water. 2 drops 2% ethanol solution of iodine for contact period of 20 - 30 min are sufficient.

→ Filtration — Ceramic filters such as Chamberland, Berkefeld filter, Katadyn filter.

→ 2.5 gram of bleaching powder is required for 1000 L of water while 2.5 gram chlorine tablet is required for 100 L of water

Hardness of water

- Hardness of water is classified as carbonate & non-carbonate hardness :

- Carbonate hardness is also called temporary hardness

as it is removable. It is d/to bicarbonates of calcium, and magnesium.

2. Non-carbonate hardness is permanent. It is d/to sulphates/chlorides, or nitrates of calcium & magnesium.
- Hardness in water is expressed in terms of meq/L. One meq/L of hardness producing ion is equal to 50 mg CaCO₃ (50 ppm) in one litre of water.
- The term soft and hard water are used when the levels of hardness are as given below:

Classification	Level meq/L	mg/L
Soft	<1	50 mg/L
Moderately hard water	1-3	50 - 150 mg/L
Hard water	3-6	150-300 mg/L
Very hard water	>6	>300 mg/L

- Drinking water should be moderately hard. Softening of water is recommended when the hardness of water exceeds 3 meq/L (>150 mg/L).
- Permutit process (base exchange methods) and addition of Na₂CO₃ removes both type of hardness.
- Fluoride level in drinking water should be 0.5 - 0.8 mg% or ppm (<1 ppm)
Defluoridation is done by Nalgonda Technique (using phosphates)
- Dry weather flow** : average amount of sewage which flows through the sewerage system in 24 hrs.
- Sewage** : - waste water + excreta
After primary sedimentation of sewage organic matter settles down and is called *sludge* & fatty layer which floats is called *scum*.
- Water source should be ≥ 15 m (50 feet) away from latrine.
- Sullage** : Waste water not containing excreta (e.g. outflow from kitchen, bathroom)

INSECTICIDES

- Resistance to HCH-dieldrin has not been developed.
- Resistance to Insecticides has not been developed in *Glossina*.
- Resistance to DDT has not been developed in *sandfly*.
- % of para-para isomer in DDT is 70-80%
- Insecticide for phlebotomus (sandfly) \rightarrow DDT
- Least toxic organochlorine \rightarrow DDT
- Least toxic organophosphorus compound \rightarrow malathion
- Synthetic pyrethroids --- Cypermethrin, proparthin, flumethrin

- Space spray**: Pyrethrum extract, malathion, fenitrothion



USED IN ULV (ULTRA-LOW VOLUME) FOGGING

- Larvicidal measures include** --- Paris green, use of mineral oil (kerosene)
- Anti adult measures include** --- Space spray, Residual spray, Genetic control
- Paris green (larvicidal)**
Stomach poison which kills mainly anopheles larva
- Abate in concentration 1mg/L & Cl₂ in strength 5 PPM is able to destroy cyclops. Most satisfactory permanent method of controlling cyclops in drinking water is to provide piped water supply or tube wells

Insecticides used for control of arthropods

Group	Class	Examples
Contact Poisons : Natural	Natural	Pyrethrum, rotenone, nicotine, mineral oils, derris
Contact Poisons : Synthetic	Organo - Cl ₂ compounds	DDT, BHC, Lindane, dieldrin, kepone, mirex
	Organo - phosphorus compounds	Chlorthion, diazinon, parathion, ronnel, gardona, abate, fenitrothion etc.
	Carbamates	Dimetilan, propoxur, carbaryl, pyrolan
Repellents		Metadi-ethyltoluamide, indolane, benzyl benzoate,
Synthetic pyrethroids		Resmethrin, proparthin, etc.

\rightarrow Temefos (abate) is used by MCD workers for mosquito control in coolers.

\rightarrow *Gambusia affinis* and *Barbados millionis*, and *Lebister reticulatus* are used for --- Biological control of mosquitoes (Kills larva of mosquitoes)

- Control of mosquitoes** :

WHO recommends minimum number of 156 holes in mosquito net per inch square area.

- Speed of flies** :

Fly	Speed in miles /hr	Speed in km /hr
Butterfly	12	
Mosquito	1.2	
Housefly	4.5	7.2
Sandfly	0.65 - 7 m/sec	

Disease transmitted by Flies

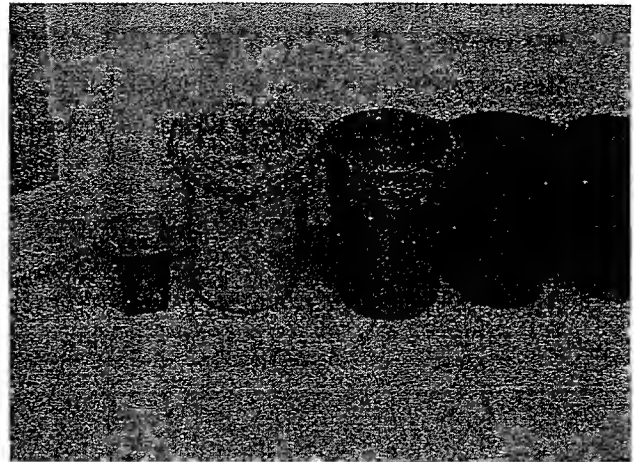
D/s	Caused by	Transmitted by (vector)
Kala-azar	Leishmania donovani	Sandfly (Phlebotomus)
Oncocerciasis	Onchoceria volvulus	Black fly (Simulium)
Chagas disease	Trypanosoma cruzi	Reduvid bug
Sleeping sickness	Trypanosoma brucei	Tse Tse fly (Glossina)
Oraya fever	Bartonella bacilliformis	Sand fly
Trench fever	Bartonella Quintana	Body lice (louse)

Disease transmitted by Mosquitoes

Mosquito	Charac-teristic	Breeds in	D/s transmitted
Anopheles	Eggs: Boat shaped, singly laid, No siphon tube in larva		Malaria Filaria
Aedes	Cigar haped eggs, Tiger mosquito	Artificial collection of water	Filaria Dengue, Rift valley fever, Chickungunya, YF
Culex	Eggs in clusters, Nauseance mosquito	Dirty water	JE, Bancroftian filariasis Polyarthrititis (viral) West-Nile fever
Mansonia		Aquatic vegetations	Malayan/Brugian filaria, chikungunya

Disposal of Biomedical/ Hospital Waste (BMW) & Color coding system

Colour of Bag	Waste Category	T/t option
Puncture proof container	Used needles, syringes, scalpel, blades, glass that may cause puncture/ sharp objects	Additional Destruction / Shredding
Yellow	Human anatomical wastes (body parts/pathological tissues), animal carcasses, microbio & solid wastes.	Incineration / deep burial
Red	Disposable tubings, catheter, IV sets, cotton, dressings, contaminated with blood/body fluids	Autoclaving / Microwaving / Chemical T/t
Blue	Wrappers of gloves/ wrappers of syringes, Gloves/plastic items	
Black	General non-infectious waste, Office papers, kitchen waste, Incineration ash, chemicals, Discarded medicines / cytotoxic drugs. (All scrap)	Disposal in secured, land fill



- Previously only 4 containers were used but Now a days 5 containers are recommended (the latest addition is blue bag).

Container or bags are NOT required for disposal of

- Liquid waste
- Chemical waste
- Locally disinfected microbiology and biotechnology waste

Inertization

- Mixing of BMW with cement and other substances before disposal.
- Suitable for pharmaceuticals and other heavy metal compounds

→ Mercury is best disposed off by --- Safe collection and recycle

→ HIV +ve patient is being infused amphotericin B for systemic fungal infection of i/v canula. Tubing should be disinfected in 1% hypochlorite and disposed off in blue bag for destruction/ shredding.

→ HIV +ve patient is being changed his dressings soaked in blood. Appropriate method of discarding is pour and disinfect in 1% hypochlorite, disposed off in red bag and send it for incineration.

Disasters in India

- Northern mountain region including the foot hills are prone to --- Snowstorm, land slides & earth quakes
- Eastern costal areas (AP, WB, Orissa) are prone to --- Severe floods and cyclones.
- Western desert areas are prone to --- Draughts.

- In post disaster phase ---
 - M/c reported d/s is gastroenteritis
 - **Measles vaccine is the vaccine recommended**
- World's worst man made disaster is Bhopal gas tragedy.
 - In the federal structure of India, the state Govt. are responsible for execution of relief work in wake of natural disasters.
 - At the centre, the ministry of agriculture is the nodal ministry for coordination of all activities during a natural disaster.

Different States with Significant Problems in India

- In West UP --- Most cases of AFP
 - In Tamilnadu --- Most cases of HIV (40% of India), Donovanosis, Madura foot
 - In Rajasthan --- Most cases of dracunculiasis reported in the past.
 - In Bihar --- Most cases of Kalazar, leprosy in the past
 - In Karnataka --- Most cases of KFD
 - Chhattisgarh --- Most cases of sickle cell anemia
 - In Punjab --- Hemoglobin - D is prevalent
 - Manipur --- Most affected area of endemic goitre
- Six states have been given national award for achieving elimination of leprosy both at district and state level, these are --- Nagaland, Himachal Pradesh, Mizoram, Tripura, Haryana, Meghalaya
 - Dracunculiasis has been eradicated from India (since 2000)
 - VHG (Village Health Guide) scheme is NOT present in J & K.
 - Sub himalyan belt is most affected endemic zone of goitre (IDD).

PNEUMOCONIOSIS

- Latency period to develop
 - CWP is 15-20 yrs
 - Asbestosis is 10 yrs
 - Silicosis is 10 months to 14 yrs
- Dust particle of the size of 20 μ or more are trapped in oropharynx.
- Dust particle within the size range 0.5 – 3 μ are health hazard for pneumoconiosis.
- Caplan syndrome is pneumoconiosis + RA
- In textile/cotton industry, there are 2 types of workers--- spinners and weavers. Spinners are prone for Byssinosis.

D/s	D/to inhalation	Feature
○ Silicosis	Silica & SiO ₂ exposure (in mica mines)	- A/w TB (silicotuberculosis) - Dense nodular fibrosis - Fibrosis in hilar LN - Nodules in UZ (upper zone) - M/c & oldest pneumoconiosis - Notifiable under factory act & mines act
○ Anthracosis (CWP)	(in coal workers)	- Progressive massive fibrosis - Notifiable under mines act
○ Byssinosis	Inhalation of cotton fibre (in spinners of textile industries)	- Monday chest tightness is the m/c symptom
○ Bagassosis	Inhalation of sugar cane dust	- Caused by thermophilic actinomycetes (<i>Thermoactinomyces saccharii</i>)
○ Asbestosis	(90% by serpentine variety) Iron / cement	- Affects lower lobes of lungs - <u>Mesothelioma of pleura & peritoneum</u> - Ca- bronchus - Retroperitoneal fibrosis
○ Farmer's lung	- Inhalation of mouldy hay/grain dust	- Caused by growth of thermophilic actinomycetes <i>micropolyspora faeni</i>

FLUOROSIS

- Fluoride level in drinking water should be 0.5- 0.8 mg% or ppm.
- Max^m permitted level of F⁻ in drinking water is 0.8 mg/L
 - Level > 1.5 ppm : Dental fluorosis
 - Level 3-6 ppm : Skeletal fluorosis
 - Level >10 ppm : Crippling fluorosis
- **Maidon teeth**
- Fluorine is considered as "Double edged sword". Inadequate intake is a/w dental carries while excess intake is a/w fluorosis.
- Nalgonda technique is for defluoroidation of drinking water.

IDD (Iodine Deficiency Disorders)

- To prevent IDD, iodine content in iodized salt at production point should be 30 ppm & at least 15 ppm at consumer level
- Iodine deficiency is common in sub himalyan belt.
- K⁺ iodate is fortified in iodized salts.
- Daily requirement of iodine in adult is > 150 μ g.

- c Double fortified salt (DFS) contain **iodine + iron**. 40 µg of iodine and 1 mg of iron per gram of salt.
- c Iodized salt is most widely used prophylactic measure against prevention of goiter.
- c **Epidemiological assessment of IDD : Indicators**
 - Prevalence of goitre (when >10% it is considered a major public health problem)
 - Prevalence of cretinism
 - Urinary excretion of iodine
 - TFT (T₄, TSH)
 - Prevalence of neonatal hypothyroidism.

→ In iodized salt Potassium iodate is fortified

→ In double fortified salt, iron is also added as ferrous sulphate with sodium bisulphate or as ferric ortho-phosphate without causing colour changes.

→ Vanaspati Ghee is fortified with vit. D (2500 IU) & vit. A (175 IU) per 100 mg.

NUTRITION

Food-borne intoxications

- c **Neurolethyrism** : Gradual spastic paraplegia d/to consumption of khesaridal. Parboiling (better) & steeping methods can prevent the risk of d/s. Vit C is also helpful.
- c **Epidemic dropsy** : Acute non-inflammatory swelling of leg is the first sign. Diarrhoea, glaucoma can be seen but convulsions are uncommon.. Death is d/to CHF. Pyruvic acid levels are ↑ ed in blood. Nitric acid test is +ve. **Paper chromatography** is most sensitive.

D/s	Adulterant	Toxin	Remark
Lathyrism	Khesari Dal (<i>Lathyrus sativa</i>)	BOAA	Gradual spastic paraplegia
Epidemic Dropsy	<i>Argemone mexicana</i> oil	Sanguinarine → Inhibits transmembrane Na ⁺ - K ⁺ protein function	↑Pyruvic acid in blood
Endemic ascites	Crotolaria/ jhunjhunja seeds	Pyrrolizidine alkaloids	Hepatotoxin
Aflatoxicosis	<i>Aspergillus flavus</i>	Aflatoxin	
Ergotism	Claviceps fusiformis	Clavine alkaloids	

Tests on Milk

Type of milk	Test done	Purpose
Fresh milk	Methylene blue reduction test	Done before pasteurization
Pasteurized milk	Phosphatase test	To check efficiency of pasteurization
	Standard plate count	Determines bacteriological quality of pasteurized milk
	Coliform count	Post pasteurization contamination

- c **Turbidity test** (in which NH₄ SO₄ is used) differentiates between pasteurized and sterilized milk.
- c **MBRT** (Methylene blue reduction), Resazurin, triphenyl tetrazolium bromide & Phosphatase test are also used to check bacteriological quality of milk.

Milk Vs Egg

Points	Milk	Egg
Rich in	Protein, calcium & vitamins (retinol, vit D)	Almost all nutrients
Poor/ deficient in	Iron, vitamin C, Vitamin E	Carbohydrate, vitamin C
Calorie	67 kcal/100 mL	
NPU	75	91
BV	85	94
AA score	3.5gm protein/100 ml in cow milk & 1gm protein/100 ml in breast milk	100 Contain all essential amino acids so it is considered as reference protein
Remark	Complete food	Reference protein

Comparative nutritive value of various milks

Nutrient	Buffalo milk	Cow milk	Goat milk	Breast/ Human milk
Fat (g/100g)	6.5-8.8	4.1	4.5	3.4
Protein	4.3	3.2	3.3	1.1
Lactose	5.1	4.4	4.6	7.4
Calcium (mg)	210	120	170	28
Iron (mg)	0.2	0.2	0.3	
Calorie (kcal)	117	67	72	65

- Human milk contain more vit C (3mg/100ml) than cow milk (1mg).
- Milk is a good source of all vitamins except vit C.
- Milk is the best and most complete of all foods.
- Egg protein is considered as 'reference protein'.
- Cut off weight of an Indian reference man is 60 kg and reference woman is 50 kg.
- Daily consumption of cranberry juice is found to prevent UTI.
- Meat is rich in iron, zinc, phosphorus.
- Fish liver oil (Halibut liver oil) is the richest source of Vit -A & Vit D.
- Fish is a good source of calcium.
- Omega 3-PUFA in fish is protective against cardiovascular diseases.

Prudent diet recommended by WHO

- Dietary fat 15-30% (ICMR 20%).
- Saturated fat <10%.
- Salt should be < 5gm/d.
- Protein 10-15 % of daily energy intake.

→ Atkin's diet is low carbohydrate diet. Used for weight reduction programmes.

Iron

- Max^m iron is found in :
Raisin (Kismis) > (Pista) > dates > cashew > almond.
Among nuts pista contain
- Fetal iron requirement is 75 mg/kg.

Calcium

- Most cereals are generous providers of calcium, and the millet "ragi" is particularly rich in calcium.
- Milk and milk products are best natural sources for calcium. (Rice is deficient in calcium)
- Limiting factors in calcium absorption are
 - Oxalate
(Present in green leafy vegetables e.g. spinach, amaranth)
 - Phytate present in millets.

- Vitamin C present in citrus fruits, ↑ calcium absorption.
- Garlic is a rich source of selenium.
- Ragi is a rich source of calcium & iodine.
- Jaggery is rich in iron.

Protein requirement in gm/kg/d

0 — 3 mth	↓	12 mth	↓	3 yrs	↓	12 yrs	↓	Adolescents	↓	Adults, pregnancy
2.3		1.7		1.83		1.50		1.30-1.40		1
Remember										
simply 2.25		1.75		1.75		1.50		1.25		1

Protein content of

Rice	Wheat	Pulses	Mixed Pulses	Meat	Soya been
6%	12%	18%	24%	30%	42%

[Remember : Chawal / Gehoon / Daal / Mix Daal / Meat /-/
Soyabeen = 6 / 12 / 18 / 24 / 30 / -/-/42]

Limiting amino acids

- In cereals --- Lysine
- In wheat --- Lysine + threonine
- In maize --- Tryptophan + Lysine
- In pulses --- Methionine (+ Tryptophan)

- Single most sensitive test for iron deficiency status : Serum ferritin (most sensitive indicator of anemia in community).
- For epidemiological assessment of iodine deficiency disorders (neonatal hypothyroidism) recommended parameter in surveillance --- Urinary excretion of iodine.
- Coconut oil is deficient in EFA,
- All "cereals" lack lysine (wheat lacks threonine also).
- Pellagra is common in the regions where maize is staple food (Niacin synthesis does not occur d/to lack of tryptophan).
- Maize protein are deficient in tryptophan + lysine
Excess of Leucine is a cause of niacin deficiency (Pellagra) in Jowar & Maize eaters.
- Roots & tubers are deficient in Methionine.
- Pulses (peas / beans etc) are deficient in Methionine + Tryptophan.
- Rice proteins are superior to wheat & maize (among cereals it contains maximum lysine)

Fats

- Lenoleic acid is maximum in --- Safflower oil
- Most important essential fatty acid (EFA) is Lenoleic acid as it can synthesize both lenolenic acid and arachidonic acid.
- Most unsaturated EFA is arachidonic acid.

- Fish oil is rich in ω :3 FA eicosapentanoic acid.
- *Sunflower oil* is rich in PUFA (65%)
- *Cocconut oil* is rich in SFA (92%). Although it is deficient in EFA, it contains medium chain triglycerides (MCT) which are directly absorbed in malnourished children.
- Docosa hexanoic acid (DHA) is characteristically present in breast milk & is essential for the growth of brain.

VITAMIN A DEFICIENCY

- The presence of any of the criteria in children b/n 6months to 6 years should be considered a public health problem

Retinol level <10 μ g/dl in	NB (night blindness)	Bitot's spots	Corneal Ulcer	Corneal Xerosis / Keratomalacia
>5%	>1%	>0.5%	>0.05%	>0.01%

[Mnemonic : ReNBUX = 5/1/.5/.05/.01]

- Vitamin A deficiency is the **m/c** cause of preventable blindness in children.
- *Vitamin A prophylaxis for prevention of nutritional blindness programme* is a part of strategy to \downarrow prevalence. It ensures supplementation of 5 megadoses of vitamin A in form of **oral retinal palmitate** given at 6 monthly interval to children b/w **9 months – 3 years**. After 2006 this programme is an integral component of RCH and thus of NRHM.

Dosage

At 9 months of age

(With measles) --- 1 lakh IU (55 mcg) retinol palmitate orally

1-5 year --- 2 lakh IU (110 mcg)

- Another schedule is as integrated with the immunization programme. 1st dose of Vit. A is given along with measles vaccine and the 2nd dose is given during DPT – 1st booster. 3rd, 4th and 5th doses are given at the age of 2 yr, 2 ½ yr and 3 yr respectively
- For the t/t of **diagnosed vitamin A deficiency or xerophthalmia** e.g. in **PEM**, dosage of i.m vitamin A (inj. Aquasol) are half of the oral dosage.

Category	Immediately	→Next day	→ After 2-4 wk
< 1 yr or < 8 kg	1 lakh IU	1 lakh IU	1 lakh IU
> 1yr or >8 kg	2 lakh IU	2 lakh IU	2 lakh IU

- In keratomalacia, another schedule is 5000 I.U. / kg/ d x5d, followed by 25,000 IU/ till recovery.
- Daily reqt of vitamin A is 1500 IU or 500 μ g / d.

→ A 6 yr old child is suffering from vitamin A deficiency, the dose of vitamin A would be ---2 lacs IU i/m.

Daily requirement (in terms of RDA) for Indians suggested by ICMR

Nutrient	RDA in pregnant female	RDA in lactating mother	RDA in normal adult	RDA in children
Calorie	+350	+600 (0-6 mo), +520 (6-12 mo)		110 kcal
Protein	+ 15 g	+25 g (0-6 mo), +18 g (6-12 mo)		
Calcium	1200 mg	1200 mg	600 mg	
Iron	38 mg	30 mg		
Vit A	800 μ g	950 μ g	350 μ g	600 μ g
Vitamin B ₁₂	1mg	1.5mg		
Folic a.	400 μ g	150 μ g		

- During pregnancy mother should consume +25% calories & +25 gm protein.

→ Vitamins whose requirement do not \uparrow in pregnancy --- Vit B₁₂, Vit A, Pantothenic acid, Vit. C, Niacin

→ Requirement does not \uparrow in lactation --- Iron and pantothenic acid

→ Higher content of certain amino acids (cystine and taurine), long chain polyunsaturated (LCPS) fatty acids like arachidonic acid and docosahexaenoic acid and lactose in the human milk promotes faster development, maturation and myelination of human brain.

→ In 1st yr of life calorie intake is base on weight

Catch-up growth during childhood, intakes should be based on age (ICMR standard)

Indicators of malnutrition in assessing the nutritional status of a community

- Maternal nutrition --- Birth weight (The percentage of newborn less than 2500)
- Infant and preschool child nutrition --- Proportion of breast fed infants, Mortality in the age group 1-4 yrs
The index, weight for height of preschool children
- School child nutrition --- The index weight for height of school children.

IMPORTANT FOOD POISONINGS

Food poisoning	Staphylococcal	Bacillus cereus	Cl. perfringens (welchii)	Cl. botulinum	Salmonella (typhimurium)
o I.p.	1-6 hr	1-6 hr	8-16 hr	24-36 hr	24-72 hr (usually 12-24 hr)
o Toxin	Preformed <u>intradietitic</u> enterotoxin which is heat stable	Enterotoxin formed in food or in gut	Spores survives after cooking and produce α , q toxin	Preformed <u>intradietitic</u> toxin A, B, E (heat-labile)	Toxin causes superficial infection of gut
o Source	Milk and dairy & bakery products, meat, salad	Fried rice	Meat, meat dishes, poultry products	Preserved / canned foods, home made cheese	Animal, egg/ poultry products rats/ mice
o Cl/F	V→D (fever usually -nt)	V→D (fever-nt) cramps +	D (+++) V± (fever-nt) cramps +	g.i. symptoms minimal dysphagia, diplopia +nt	Fever +nt Acute colitis
o Remark	[V = Vomiting, D = Diarrhoea]	Diarrhoeal form have i.p. of 12-24 hours	-	Conscious, no fever	-

- Enterotoxins are usually exotoxins.
- Staphylococcal FP is commonest FP.
- Fever is absent in staphylococcal, bacillus cereus, clostridium perfringens and botulinum.
- Intradietetic (preformed) toxin is seen in staphylococcal FP and botulism.
- Diarrhoea and lower g.i. symptoms predominate in clostridial perfringens, Cl difficile, vibrio cholera (D → V) and Campylobacter jejuni.
- Pickled/canned foods & vegetables are m/c cause of botulism.

HEALTH AGENCIES & COMMITTEE

Recommendations of some committee

1. Bhore Committee, 1946

- o Integration of preventive & curative services.
- o Establishment of PHC in 40,000 population in rural areas (short term measure).
- o Setup of long term programme (3 million plan)
- o 3 months training in PSM for interns to prepare 'Social Physicians'.

2. Mudaliar committee, 1962

- o Advised strengthening of existing PHCs and also district hospitals.
- o Each PHC should not serve >40,000 population.
- o Constitution of all India health services on the pattern of Indian administrative services.

3. Chadah Committee, 1963

'Vigilance' operations in respect to NMEP (Malaria eradication). Concept of MPH was introduced first time.

4. Jungalwala Committee, 1967

Defined integrated health services.

5. Kartar Singh, 1973

Concept of FHW & MHW in place of ANM

6. Shrivastav Committee, 1975

- o It was a group on medical education & manpower support
- o It recommended creation of paraprofessionals and semiprofessionals
- o Development of 'Referral services complex'.

→ In India a new approach to health care (k/as primary health care) system came into existence following international health conference at Alma Ata

- o Extended sickness benefit is given for 309 days
- o In ESI scheme employer's contribution to the PF is 4.75%

Assisting agencies

- o SIDA --- in TB + Leprosy
- o DANIDA --- in Blindness control + Leprosy
- o CARE --- in Midday meal program.
- o UNICEF --- in GOBI campaign for breast-feeding, GOBI-FFF stress is given on female education, FP, food supplementation
- o Ford foundation --- in Rural health & family planning.

- Primary health care as a principle of WHO was founded at Alma ata (Russia) conference in 1978.
- "Health for all" concept announced by WHO at Geneva
- Health and immunization are primary responsibilities of State.

Headquarters & establishments

- UNESCO --- Paris
- UNICEF --- New York (established in 1946)
- WHO --- Geneva (established in 1947)
- FAO --- Rome

Important National Institutes

- National institute of epidemiology --- Chennai
- National institute of occupational health --- Ahmedabad
- National institute for the physically handicapped --- New Delhi
- National institute for the mentally handicapped --- Secunderabad
- National institute for the hearing handicapped --- Mumbai
- National institute for the Visually handicapped --- Dehradun
- National tuberculosis institute --- Bangalore

Red Cross

- Red cross was founded by Henry Dunant
- In Red cross emblem, size of bars is equal horizontally and vertically.
- Convened in Geneva
- Misuse is a punishable offense.

Various ministries assisting in health programmes

- Health & Family Welfare (MOHFW)
 - Vit. A prophylaxis,
 - Nutritional anemia prophylaxis,
 - IDD control
- Social welfare
 - Special nutrition program,
 - Balwadi nutrition program,
- M/O Women and Child development (MOWCD), a subset under HRD ministry
 - ICDS program
- Ministry of education
 - Midday meal program

- Mid day meal programme meal should provide 1/3rd of calories and 1/2 of proteins of the daily requirement (protein is more important).

Union Ministry of Health & Family Welfare :

Functions are:

Union List: Function are

- (i) International health relation
- (ii) Administration of Central Institutes
- (iii) Promotion of research
- (iv) Regulation and developments of medical, dental, nursing
- (v) Establishment and maintenance of drug standards
- (vi) Census collection
- (vii) Immigration and emigration
- (viii) Regulation of labour
- (ix) Coordinate with other ministries

Concurrent List:

- (i) Prevention of spread of communicable diseases
- (ii) Prevention of adulteration
- (iii) Control of drugs and poison
- (iv) Vital statistics
- (v) Labour welfare
- (vi) Population control and family planning
- (vii) Social and economic planning

Kyoto Protocol

- Measures related to ↓ global warming (Green house effect) by reducing emissions to <5.2%
- Stratosphere ozone is not harmful but it protects from harmful UV rays.

Management methods and techniques

Methods based on behavioural sciences	Quantitative Methods based on
Organisational Design	Cost benefit analysis, cost effective analysis, cost accounting
Personal management	Input-output analysis, System analysis
Communication	Model
Information system	Network analysis - PERT and CPM
Management by objectives	Planning-programming-budgeting system (PPBS) Work sampling Decision making

IMPORTANT DATES / DAYS

- 1st week of May -- Malaria week in India
- 2nd week of May -- Thalassemia week
- 1st week of August -- World Breast Feeding Week.
- 2nd Wednesday of October -- World Disaster reduction day.
- 1st May : World labour day
- 30th Jan. : Anti-Leprosy day
- 24th Mar : World tuberculosis day
- 7th April : World Health day (WHO day)
- 2nd Sunday of May : Mother's day
- 31st May : No tobacco day / No smoking day
- 5th June : World environmental day
- 11th July : World population day
- 1st July : Doctor's day
- 16th Oct. : World Anaesthesia day
- 14th Nov. : Children's day, World diabetes day

- 1st Dec. : AID's day (*remember AID s : At 1 Dec.*)

- *Census - 1st census in 1881, conducted at 10 yrs. interval at the end of 1st quarter (March end or 1st April) of the 1st year of decade*
- *Mid year population is calculated from 1st July (at the end of 1st half of the year)*
- *Sample registration system (SRS) - Birth & death survey are done at 6 months.*

IMPORTANT YEAR

- 1948 : India joined WHO as a member state, ESI act.
- 1951 : 1st Five year plan started
- 1952 : Community development program, PHC set up.
- 1953 : National Malaria control program. Family planning program.
- 1957 : Influenzae pandemic swept the country.
- 1958 : NMEP
- 1960 : School health committee
- 1962 : School health program
National goitre control program
District Tuberculosis program (DTP)
- 1963 : Applied nutrition program
(with aid from UNICEF, FAO & WHO)
National Trachoma control program,
Extended FP program.

- 1973 : Minimum need program.
- 1974 : Extended programme on immunization (EIP) started..
- 1975 : India became smallpox free.
- 1981 : 1st case of AIDS was recognized in USA
- 1986 : 1st case of AIDS was registered in India.
- 1994 : Transplantation of Human organs Act passed.
Epidemic of plague in Surat.
- 1997 : RCH program & 9th five year plan launched.
- 1998-99: National malaria eradication program renamed as National Anti-Malaria Program (NAMP).
National Family Health Survey - 2 conducted covering 90,000 women 15-49 years.
Phase-II of national AIDS control program became effective.
- 2001 : Empowered action group (EAG) constituted in 2001 to assist through health & family welfare program for states more deficient in socio demographic indices (UP, MP Bihar, Orissa, C.G., Jharkhand & Uttaranchal)
- 2002 : Govt. announces National AIDS prevention & control Policy 2002
National Health Policy 2002 announced.
- 2003-04: National Vector Borne Disease Control Programme (NVBDCP) was started. It includes JE and dengue/ DHF with other 3 ongoing programmes.

IMPORTANT HEALTH PROGRAMMES

National AIDS Prevention and Control Policy

In April 2002 GOI (Government of India) approved it.

- Objective is to bring about **zero transmission** rate of AIDS by year 2007. Behavioural Surveillance Survey - Carried out in all 35 states in country between April-Sept. 2001
- Prevention of HIV transmission from mother to child. Single dose nevirapine to mother and child has been started from 1st Oct. 2001 to 11 centres giving priorities to 6 prevalent states : Tamil Nadu, Maharashtra, Manipur, Nagaland, Karnataka and Andhra Pradesh.

NRHM (National Rural Health Mission)

- Launched in april 2005 by GOI.
- It seeks to provide effective healthcare to rural population with special focus on 18 weak states

- Utilizes village based **ASHA** ("Accredited Social Health Activists") who would act as a link b/w the health centres and the villagers. One ASHA will be raised from every village or cluster of villages.
- Impact indicators for ASHA are --- IMR, child malnutrition rates, no. of TB/ leprosy cases compared to prev. yr
- RCH II (Janani suraksha yojana is included in it) is integrated
- The resource person for training of ASHA under NRHM is will be.

JSY (Janani Suraksha Yojna)

- 100% centrally sponsored scheme launched on 12th April'05.
- National maternity benefit scheme has been modified into a new scheme called JSY.
- Under NRHM it integrates benefit of cash assistance with institutional maternal care. Cash benefits include Rs. 700 (1400 for LPS) in rural area & 600 (1000 for LPS) in urban area. ASHA also gets Rs. 600 in rural & 200 in urban area for motivation
- Beneficiaries are--- all BPL women of ≥ 19 yr age for first 2 live births. In low performing states, benefit for 3rd child is also considerable if she wishes for sterilization.

Kishori Shakti Yojna (Janani Suraksha Yojna)

- Launched on 16.02.2001.
- For unmarried adolescent girls (11-18 yr) who are BPL. Covers all the blocks (6118) in the country.

Blood Safety Programme-1998

- As per national blood safety policy, testing of every unit of blood is mandatory for detecting infections like **HIV, hepatitis B, malaria and syphilis**. From 1st June, 2001 it is made mandatory to test blood for HCV also.
- HEV is not known to be transmitted by BT.*

Community based universal health insurance scheme

- Launched during 2003-2004.
- Its premium comes in three different types:
 - Re 1 per day per year for an individual

- Rs 1.5 /day per year for a family of up to 5 members
- Rs 2 /day per year for a family of up to 7 members.

ESI Act

- Employer contributes 4.75% & employee contributes 1.75% of gross salary.
- The maximum duration for sickness benefit is 91 days.

National Programme for Control of Blindness (NPCB)

- Targets for tenth five year plan are
 - ↑ Cataract surgery rate to 450/ lakh
 - ↑ IOL implantation in > 80% cataract surgery
 - Development of 50 pediatric ophthalmology units
 - Facilities for early d/g and t/t of glaucoma pt.
 - Setting up 20,000 Vn centres in rural areas.
 - Development of 25 fully operational eye bank network
- Organizations which are assisting in blindness control programme: World bank, WHO, Danish

Vision 2020 : The Right to sight

- It is a global initiative to reduce preventable and curable blindness by the year 2020
- Target diseases are :

Global vision 2020 : Cataract, refractive errors low vision, childhood blindness, glaucoma , diabetic retinopathy, trachoma, age related macular degeneration, onchocercariasis.

India vision 2020 : Cataract, glaucoma, diabetic retinopathy.

National Vector Control Programme

- Covers malaria, dengue, filaria, JE, kalazar, chikengunya.

→ *NIP had included Hepatitis-B vaccination in June 2002. Under this pilot project Hepatitis-B vaccine is being administered to infants along with primary doses of DPT vaccines on 6th, 10th and 14th week. This project is already running in Delhi & NCT.*

→ *Survey of leprosy is carried out by an independent agency. "The Leprosy Mission", New Delhi in the seven high endemic states of Bihar, UP, MP, Orissa, West Bengal, Chattisgarh, Jharkhand*

→ *Transplantation of human organs act was passed in the year 1994*

Millenium Development Goals (MDG)

- Started in Sept. 2001. Targets to be achieved by 2015.

- Directed towards areas of development and poverty eradication.
- *Goals are*
 - Eradicate extreme poverty and hunger
 - Achieve universal primary education
 - Promote gender inequality
 - Improve maternal health : Reduce child mortality
 - Combat HIV, malaria, and communicable disease
 - Ensure environmental sustainability
 - Global partnership for development.
- Tenth five year plan was launched in 2003. 11th FYP was launched in 2009

SOME POINTS OF SPECIAL MENTION

- M/c cause of preventable childhood blindness worldwide
 - Vit A deficiency
- 'Haddon's matrix' term is related to --- Accidents
- Micronutrients are : Vit A, Ca, I, Iron, Zn
- In non -paralytic poliomyelitis DTR are diminished but not absent
- In family welfare program score of 1=sterilization, NRR 3=IUCD, 9=OCPs, 18=Condoms
- MCH care is assessed by : MMR
 - Living standard of people is assessed by : PQLI
 - Most universally accepted indicator of health : IMR
- Herd immunity may be determined by : serological survey (serological epidemiology).
- Hospital statistics provides only numerator not the denominator.
- Regular reporting of health statistics is done primarily to understand the trend of diseases.
- Time taken for any project is estimated by : Network analysis (CPM)
- McKeon study on tuberculosis concluded the social and environmental factors responsible for reduced prevalence of TB in 17th century.
- Sputum expectoration specimen is collected for examination of --- Mycobacteria, legionella, pneumocystis carinii.
- According to WHO blindness is visual acuity < 3/60 or its equivalent (Snellen).
- For detection of missing contact (hidden cases) ⇒ sentinel surveillance
 - Total morbidity is best assessed by ⇒ active surveillance
- Water requirement per day ⇒ 150 - 200 L (with 2 ltr of drinking water per head)

- Per capita space for students in a classroom ⇒ 10 sq.ft.
- M/c problem of elderly ⇒ Locomotor disorder
- **BIOTERRORISM**
 - Most important and potential organism is --- Small pox
 - Other imp organisms, which can be potential weapon in spread of bioterrorism are: ---
 1. Bacteria: Anthrax, Plague, TB, Q-fever
 2. Viruses: Small pox, Monkey pox, Encephalitis viruses, VHF.
 3. Toxins: Enterotoxin B of staph, Botulinum, Fungal toxins, Ricin etc.
- In network analysis longest path is -- PERT
- Porter of infection --- housefly.
- Universal precautions do not apply to following body fluids unless they contain visible blood - faeces, nasal secretions, sputum, sweat, tears, urine, vomitus breast milk, saliva.

SOME IMPT. NEGATIVE POINTS

- NOT included in health sector planning (Govt policy)--- Nutritional & food supplements
- NOT a component of Health Policy and primary health care --- Medical education .
- Iceberg phenomena is NOT seen in --- Chicken pox, Measles
- Subclinical infections are NOT common in --- Chicken pox, Measles
- NOT included in extended sickness benefits in ESI --- Syphilis & acute diseases like malaria
- NOT covered under ESI act --- Educational institutions
- NOT used as larvicide--- DDT
- Resistance to DDT is NOT shown in --- Phlebotomus
- NOT indicative of fecal pollution of water --- Staphylococci
- NOT an indicator of Pollution of water --- Fluorides (F⁻)
- NOT seen in cong. rubella syndrome --- Renal anomalies
- Healthy carriers are NOT seen in --- Pertussis
- NOT indicator of air pollution --- H₂ > CO₂
- NOT a duty of TBA --- Administering TT
- Mass chemoprophylaxis is NOT indicated for -- Scabies.
- Vaccine NOT indicated for elderly -- Measles.
- NOT a way to eliminate bias --- Multivariate analysis.
- About mass communication NOT true is --- it suits local needs
- NOT a zoonoses --- AIDS
- NOT included in IMCI --- Neonatal tetanus

- NOT a cause of indoor pollution --- Mercury vapours
- NOT an indicator of nutritional status in community --- The proportion of pregnant woman with Hb < 11.5 gm%
- Health status of a child <5 will NOT be adversely affected by --- Maternal Hb > 11 gm%
- NOT an example of analytical study --- Field trials
- Socialization of medicine does NOT leads to --- Ensures complete utilization of services by all the people.
- For which intervention unit is NOT an individual --- Health education.
- NOT a part of primary health care --- Cost effectiveness
- NOT a synthetic pyrethroid --- DDT
- Sputum can NOT be disinfected by --- Chlorhexidine
- Was NOT a factor for Small pox eradication --- Cross immunity with animal pox viruses
- NOT true of redcross amblem --- C/b used by UNO
- NOT true of MMR --- Denominator includes stillbirths and abortions
- Ressurgence of Malaria is NOT due to --- Host genomic variation, antigenic variation in parasite.
- NOT true of Lepromin test --- It is used for diagnosis of leprosy.
- Arboviral disease which is NOT endemic in India --- Yellow fever.
- NOT suggested in WHO report 2008 --- Setting up of economic reforms.
- NOT included in screening under national health programme --- Diabetes mellitus.
- NOT true of NRHM --- Setting up of primary health care units.
- NOT a principle of EBM (evidence based medicine) --- Depends upon clinical model and decision analysis to base its recommendations.
- Socialization of medicine does NOT include --- Ensures complete utilization of health services by all people.
- In Hardy- Weinberg's law equilibrium is NOT affected by --- Random mating.
- NOT a founding member of vision 2020 --- UNICEF

CLINICAL VIGNETTES

- A study was conducted on carcinoma colon. The study revealed lesser incidence of carcinoma colon in pure vegetarians than non-vegetarians by which it was concluded that β carotene is protective against colon cancer. This may not be true becoz the vegetarian subjects may be consuming high fibre diet which is protective against cancer. This is an example for :

- A. Causal association
 - B. Common association
 - C. Multifactorial association
 - D. Confounding factor [AIIMS Nov'10]
- (Ans: D. Confounding factor)

- Confounding factor is one which is a/w both exposure and d/s but distributed unequally in study group and control group resulting in confusion /bias in the outcome.
- In multifactorial causation many risk factors act independently and synergistically to produce a causal effect.
- **Association** is simultaneous existence of 2 variables. If association imply a causal relationship b/w variables it is k/as causal association.

- In a certain population, there were 4050 total births last year, of which 50 were still births. 50 infants died within 7 days of birth whereas 150 more infants died within 28 days. What is the neonatal mortality :

- A. 50
 - B. 62.5
 - C. 12.5
 - D. 49.4 [AIIMS Nov'10]
- (Ans: A. 50)

$$\begin{aligned}\text{Total no. of livebirths} &= \text{Total birth} - \text{still births} \\ &= 4050 - 50 \\ &= 4000\end{aligned}$$

$$\text{Neonatal mortality} = \frac{\text{Early neonatal deaths (<7days)} + \text{Late neonatal deaths (<28days)}}{\text{Total no. of live births in the same yr}}$$

$$\begin{aligned}\text{NMR} &= 200 \times 1000 / 4000 \\ &= 50 \text{ per } 1000\end{aligned}$$

- In UK, a study was conducted on population. An association was found between sale of antiasthma drug and increase in deaths due to its side effects of these drugs. This is an example for :

- A. Ecological study
 - B. Cohort study
 - C. Case reference study
 - D. Experimental study [AIIMS Nov'11]
- (Ans: A. Ecological study)

Ecological studies are conducted on group of people or population while rest of the studies given in options are conducted on individuals.

MEASURES OF CENTRAL TENDENCY

- Arithmetic mean
- Median
- Mode
- Geometric mean (used only for +ve value)

$$GM = \sqrt[n]{x_1 x_2 x_3 \dots x_n}$$

Arithmetic mean (simply 'the Mean')

- Most useful statistical average when performing analytic manipulations. $\bar{x} = \frac{\sum x_i}{n}$
- Sensitive to an extreme value in series

Mode

- Most commonly occurring value in a distribution of data's
(Most fashionable value in series of observations)
- Useful in practical epidemiological work (calculations of incubation period), business statistics
- Most difficult measure of central tendency to manipulate mathematically,
- Mode is roughly equal to mode = 3 median - 2 mean

Median

Data's are first arranged in increasing or decreasing order & the central value (5th value in a series of 9 values) is median. In case of even numbers of total values (e.g. 10) average of 2 middle most values (5th & 6th values) is median. It corresponds middle of quartiles & middle of percentiles

Standard error

$$(SE \text{ or } \sigma_{\bar{x}}) = \frac{\sigma}{\sqrt{n}}$$

The standard error is dependent on the size of the samples: Standard error is inversely related to the square root of the sample size.

Results of large studies or surveys are more trusted.

Z score (Standard Score)

The z score is calculated in terms of the number of standard errors by which a sample mean lies above or below the

population mean. Calculated for normal distribution.

$$z = \frac{X - \mu}{\sigma} \text{ now becomes } z = \frac{\bar{X} - \mu}{\sigma_{\bar{x}}}$$

Estimated standard error of the mean

$$\sigma_{\bar{x}} = \frac{S}{\sqrt{n}} \text{ where } S \text{ is the sample standard deviation}$$

Central Tendency in Various Distributions

Distribution	Central tendency
Normal (Gaussian) distribution	Mean = Median = Mode (all 3 coincide)
Right (positive) skewed distribution	Mean > Median > Mode
Left (negative) skewed distribution	Mean < Median < Mode

- In a bimodal distribution, Mode = 3 median - 2 mean. Bimodal distribution of age and incidence of d/s is seen in Hodgkin's lymphoma, leukemia, nasopharyngeal carcinoma and female breast carcinoma
- In a distribution with extreme values — Mean is the measure of central tendency which is most affected, Mode is least affected, and median is most preferred measure.

Pearson's coefficient of skewness

$$CS = \frac{(\text{Mean} - \text{mode})}{SD} = \text{Pearson's mode}$$

$$CS = \frac{3(\text{Mean} - \text{median})}{SD} = \text{Pearson's median}$$

Centiles (percentiles)

- Percentiles are values in a series of observation arranged in an ascending order which divides a distribution into 100 equal parts
- Commonly used in growth charts. WHO growth charts uses 50th percentile as upper line of growth curve while 3rd percentile for lower reference curve.

Quartile

- Divides a distribution in 4 equal parts. So the number of intercepts are 3 Q1, Q2, Q3. So 25% values are covered b/w 0 to Q1, next 25% values are covered b/w Q1 to Q2 and so on.
- First quartile Q1 divides a distribution in a ratio of 25: 75 Second quartile Q2 divides a distribution in a ratio of 50:50. Thus Q2 is equivalent to median

Third quartile Q3 divides a distribution in a ratio of 75: 25

Tertile

- Divides a distribution in 3 equal parts.

Confidence limits

The limits of ± 1.96 standard errors are called the confidence limits.

MEASURES OF DISPERSION / VARIABILITY

Characteristics that are used to describe spread / variability of individual observations & scatter of a series of values.

These are :-

- Range
- Mean deviation or average deviation
- Standard deviation (SD or σ)
- Quartile deviation (Semi-inter quartile range or Q)
- Coefficient of Variation (COV)

Range

- Difference b/w highest and lowest value (consider midpoints of extreme of data when grouped data are taken)
Normal range is the range of mean ± 2 SD
- Simplest measure of dispersion
- Provide no information concerning scatter within series

Mean Deviation

Average of deviations from arithmetic mean

$$MD = \frac{\sum(X - \bar{X})}{n}$$

S.D.

- Root - Means - Square deviation. Most frequently used measure of deviation.
- Sum of squared deviations from mean / No. of value-1

$$SD \text{ or } \sigma = \sqrt{\frac{\sum(X - \bar{X})^2}{n}} \quad (n-1 \text{ if sample size is } < 30)$$

Variance

- Sum of squared deviations from mean / No. of value-1

$$V = \frac{\sum(X - \bar{X})^2}{n-1} = SD^2$$

SD is the positive square root of variance. $SD = \sqrt{+V}$

Standard Error of Estimate

Measure of the accuracy of predictions

$$\sigma_{est} = \sqrt{\frac{\sum(Y - \bar{Y})^2}{n}}$$

Co-efficient of Variations

$$CV = \frac{SD}{\text{mean}} \times 100 \text{ or } C.V. = \frac{\sigma}{\bar{X}} \times 100$$

CV is used to compare variability of 2 distribution.

- SD is m/c and most appropriate measure of dispersion
- Standard error of difference b/w 2 means is observed by --- Interquartile range
- Standard error of difference b/w 2 proportions is observed by ---SD

MEASURES OF CHANCE

Characteristics that are used to measure chance are

- Probability
- Odds
- Likelihood ratio

Probability

- Probability of an event is the measure of the chance that an event will occur as a result of an experiment. The probability of an event A [P (A)] is the number of ways event A can occur, divided by total no. of possible outcomes.
- Probability ranges from 0 to 1 i.e. it can not be less than zero or more than 1
- Probability rules :
Rules of addition :
For mutually exclusive events (events which are dependent on each other for happening) P total = P(A) + P(B)
Rules of multiplication:
For 2 or more independent events P (total) = P(A) \times P(B)

Odds

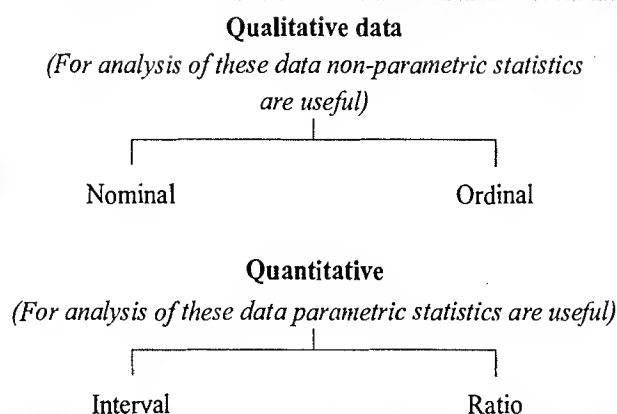
- Odds are chance of frequency of occurrence of a characteristic relative to its non-occurrence.
- Expressed as a ratio of occurrence to non-occurrence
- Odds = Probability / (1- Probability) or Probability = Odds / (1+ Odds)
- Post test odds = Likelihood ratio \times Pretest odds
- If probability of occurrence of lung cancer in a man is 0.60 then odds for lung cancer would be 1.5

Odds Ratio (OR) or Cross product ratio or relative odds

- OR is the ratio of odds that cases were exposed to a risk factor to the odds that control were exposed

- OR = ad/bc if $OR > 1$ (associated), = 1 no association, or < 1 protective effect
- OR is used to measure **strength of association in a case control study**

SCALES OF MEASUREMENT / TYPES OF DATA



	Categorical scales		Dimensional Scales
Based on	Nominal scale	Ordinal scale	Metric scale
Based on	Names (NOM) No specific order	Order (ORD) Categories	Measurement (ME) in terms of quantities
Data	Qualitative	Qualitative	Quantitative
Permissible arithmetic	Counting	> or < operations	+ / - (in interval scale) X / division (in ratio scale)
Permissible statistics	Mode, Chi-square test	Median	Mean, SD, correlation, regression, ANOVA (for interval scale) Geometric mean, coefficient of variation (for ratio scale)
Examples	Site of cancer Sex (M or F) ABO blood group Race, religion, country Site of lymphadenopathy (axillary, cervical, inguinal etc.)	Staging of cancers (TNM) Social classes (class I, II, III) Severity of d/s (stage I, II, III)	Anthropometric indicators (Height, wt, MAC) Lab values (Blood sugar, Hb%, S.cholesterol) Vitals (Pulse rate, BP, Temperature)

Discrete Vs. Continuous variables

Discrete variable	Continuous variable
<ul style="list-style-type: none"> Piece of information that can be present or absent (half or point value is not possible). E. g. Boys in classroom (50 or 51 but never 50.5) Rashes in measles (10 or 11 never 10.5) Broken leg 	<ul style="list-style-type: none"> Values are continuously distributed around mean (Normal or skewed distribution). Weight in kg, height in cm. All the data's of <u>interval scale</u> Values possible in point. (weight of the child may be 2.4 kg, 2.5 kg, or 2.6 kg)

- Confounding variables are - age, sex, social class
- Paired t test is used for continuous variables/data of interval
- Statistically most preferable scale of measurement is --- Metric scale (intervals)
- Statistically least preferable scale of measurement is --- Nominal scale

Nominal

- Used as a measure of identity
- When data's are qualitative in nature (or in group). They can't be placed in a meaningful order e.g. Division on the basis of religion, caste (e.g. Hindu/ Muslim/ Sikh or Muslim/ H/ S anything possible)
Sex (Male / Female)
Colour, Race (Black / White), Eye Colour
Rural & Urban differences (Urban / Suburban / Rural)
Marital Status, numbers on the back of athletes.

Dichotomous scale

Is a part of nominal scale in which only two variable are compared. E.g. marital status - married/unmarried

Ordinal

- In this scale **data's can be placed in a meaningful order**, but there is no information about the size of the interval.
- Ranked or arranged from highest to lowest or vice versa
Number reflects rank order of object.
Examples are :-
- Ranking of students in the class (1st, 2nd, 3rd, 4th etc.)
- Staging of cancers (Grade-I, II, III)
- Variables in the form of mild, moderate and severe.
Brightness or dullness rating.
(very bright---brighter---bright --- dull)

Opinion of people for a test (very satisfied ---satisfied
---dissatisfied--- very dissatisfied)

Harder or softer.

- For these data we can determine Median, centile, computing rank correlation coefficient.

Metric Scale Data

Interval

- These data's can be placed in a meaningful order with meaningful interval b/w them.
- Each individual has one measurement in this continuous data.
eg. *Measurement of height, weight, temperature in °C or °F (36 °C to 40 °C).*
- Data do not have absolute zero.
- These are *m/c used variables in statistics*. We can calculate mean, SD, t-test etc.

Ratio

- Same as interval but has an absolute zero. Examples are
weight scale in grams, kg; BP scale
Time in seconds, days, minutes, etc.
BP in mmHg & pulse rate.
Loudness in dB
The only ratio scale of temperature is the Kelvin scale (in which 0° indicates an absolute absence of heat, just as zero pulse rate indicate an absolute lack of pulse).

TEST OF SIGNIFICANCE

Student-t test Vs. Paired-t test

Student t test	Paired t test
Two groups are compared	Same individual / group is compared for continuous variable before T/t & after T/t. eg. : BP testing before T/t & after T/t.

- Tests of significance: - (Z test, t test & Anova test)
 - For large sample (values >30) ——— Z test is used.
 - For small sample (values <30) ——— t test is used.
- Criteria for applying Z & t tests: -
 - Sample should be selected Randomly (simple random samples) for Z & t test both
 - There should be homogeneity of variance in the two samples.
 - Variable should be normally distributed and data should

be quantitative (for t test).

- Homogeneity of variance is tested by using 'F' test.

Anova Test :

- It is useful technique for comparison of means of several groups.
- Simple one-way classification is just an extension of student t test, but here it is more than 2 groups.

Assumptions for anova test :

- Individuals in various groups should be selected on the basis of Random sampling.
- Variables under study should follow normal distribution.*
- Variables of the groups should be homogeneous (tested by using variance ratio test).*
- Samples comprising the groups should be independent.*

Hypothesis (H)

Is an assumption about the status of a phenomenon. Hypothesis is variable to be tested.

P value

P value denotes probability of the occurrence of the event by chance. If we take P value for 95% confidence intervals(limits) means we take 5% error (α).

Null Hypothesis (H_0)

When we have to prove a particular hypothesis about difference b/w 2 regimens, we make Null hypothesis. If we have to prove that the new drug is better than older one H_0 = New drug is not better than old drug.

	H_0 rejected	H_0 not rejected
Null hypothesis (H_0) is true	Type I or α error	No error
Null hypothesis (H_0) is false	No error	Type II or β error

There are 2 type of statistical (sampling) error or statistical errors based on H_0

Type-I or α error	Type-II or β error
Rejection of null hypothesis that is actually true.	Acceptance of null hypothesis that is actually false
Error of first kind	Error of second kind
It is used to determine <u>sample size</u> .	Used to determine the <u>power of a study</u> ($1-\beta$).

Probability of type I error is given by 'p value'	Probability of type II error is given by 'β'
Example : If a new drug is actually not better than old drug H_0 is true. But we reject it (it is declared that new drug is better and it is launched) it is Type I or α error	Example : H_0 is false, if a new drug is actually better than old but H_0 is not rejected (it is declared the new drug is not better than old drug and drug was not launched) it is Type II or β error
More serious error	Less serious error

- The type-II error is used to determine the "power of a study" which is equal to $1-\beta$
- The power is the "probability that the study would reject a null hypothesis as false when it is actually false".
As the sample size increases, the power of study increases.
- Type-I error is inversely related to type-II error.
- Multiple comparison & testing (for significance) increases the likelihood of type-I error.
- Most analysis are done with α error of 5% and β error of 20%.
- A test with high specificity has low rate of type I error
FP rates $\alpha = 1 - \text{specificity}$
FP rates $\beta = 1 - \text{sensitivity}$

Degree of freedom in contingency table

d.f. = $(c-1) \times (r-1)$ [c = columns, r = rows]

Visual analog Scale

- VAS is a measurement of continuous spectrum of values.
E.g. in case of pain

DATA

Methods of presentation of Data

- Tabulation --- a) Simple table, b) Frequency distribution tables
- Charts and diagrams :-
 - a) For Quantitative data:
 - i) Histogram
 - ii) Frequency polygon
 - iii) Frequency curve
 - iv) Line chart/ graph
 - v) Cumulative frequency diagram (Ogive)
 - b) For Qualitative data :-
 - i) Bar diagram
 - ii) Pie chart or sector diagram
 - c) Pictogram

d) Scatter or dot diagram

Histogram

Graphical representation of continuous quantitative data.. Continuous groups are marked on x-axis while frequencies are marked on y-axis.

Frequency polygon

Used for continuous and ordered data. It is an area diagram of frequency distribution developed over a histogram.

Frequency curve

When number of observations is large and group interval is reduced

Scatter / dot diagram

Graph showing relationship (correlation) b/w 2 quantitative variables. also k/as 'correlational diagram'

Sector diagram/ Pie chart

Representation of discrete data of qualitative nature. It represents proportional division of sample.

Pictogram/ picture diagram

Representation of data using pictures.

- Epidemic curve --- is a histogram and help to identify peak of disease, possible i.p. (mode) & type of disease propagation.

L J Charts (Levey - Jennings Charts)

- LJ chart is a graph that quality control data is plotted to give a visual indication whether a lab test is working well
- Used to determine both accuracy and precision
- On the x axis date, time or number of controls run are plotted while on y axis control data are plotted.

Distributions of data

Normal Distribution

- Also k/as "Gaussian distribution" or standard distribution.
- It is distribution of values of quantitative variables. It is a smooth, symmetrical, bell shaped curve.
- Total area of the curve is 1 (100%). 50% of the values lie above the mean and 50% value lie below the mean. ~2/3rd values under a normal distribution fall within 1 SD of the mean & ~95% fall within 2 SD of the mean.
- Mean + 1SD ($\mu \pm 1\sigma$) covers 68% values
Mean + 1.96 SD ($\mu \pm 1.96\sigma$) covers 95 % values

Mean + 2SD ($\mu \pm 2\sigma$) covers 95.45 % values

Mean + 3SD ($\mu \pm 3\sigma$) covers 99.7% values

- Mean(μ) = 0, SD(σ) = 1, variance = 1 (variance = SD^2)
= $1^2 = 1$

- Mean, median, mode all coincide.
- Standard tests based on normal distribution are k/as parametric tests. These are student 't' test and ANOVA - F test
- Skewed deviation is 0 (neither skewed to Lt nor to right).
- Distance of value from \bar{x} is called relative deviate
 $z = (x - \bar{x}) / \sigma$

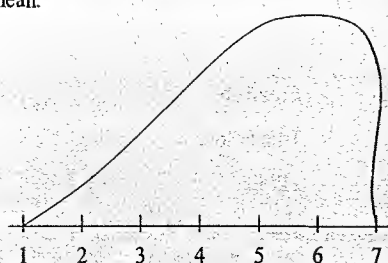
Asymmetrical / Skewed or Log normal distribution

Skewed to left (-vely skewed)

If more outlying values are smaller than the rest, data are said to be skewed to the left or negatively skewed.

Data have longer tail among lower values.

Median > mean.

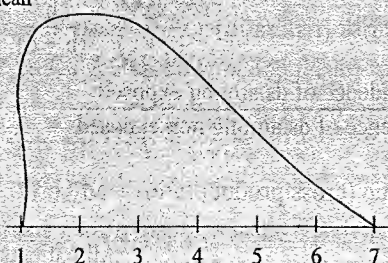


Skewed to right (+vely skewed)

When more outlying values are larger than the rest of the values data are said to be skewed to the right or positively skewed.

Longer tail among higher values.

Median < mean



→ In general if the curve is skewed, the mean is always towards the long tail, the mode near the short tail and the median somewhat between the two.

→ The median is more robust than the mean because it is less sensitive to extreme observations and is more appropriate measure of central tendency when extreme values are part of data set.

Poisson Distribution

- Limiting form of binomial distribution when probability of success is closer to zero & no. of trials are infinite.
- Mean = Variance

SCREENING TESTS

		D/s present	D/s absent	Total
Screening test	+ve	a	b	a + b
	-ve	c	d	c + d
Total		a + c	b + d	a + b + c + d

[a = TP, true positives = TP ; b = FP, c = FN, d = TN]

Sensitivity

- Is the ability of a positive test in people with the d/s

$$\text{Sensitivity} = \frac{\text{TP}}{\text{all pt with d/s}} = \frac{a}{a + c}$$

$$= \text{TP} / (\text{TP} + \text{FN})$$

- It is the diagnostic accuracy of a test
- Is the proportion of **truly ill** people in the screened population who are identified as ill by the screening test.
- A Sensitive test helps rule out d/s (when the result is negative).
[mnemonic : Sensitivity rule out or "SNOUT"]

Specificity

- Is the probability of a negative test in a non-diseased person.

$$\text{Specificity} = \frac{\text{TN}}{\text{all pt without d/s}} = \frac{d}{b + d}$$

$$= \text{TN} / (\text{FP} + \text{TN})$$

- Is the proportion of **truly healthy** people in the screened population who are so identified by the screening test.
- A very specific test rules in disease with a high degree of confidence. [Mnemonic - Specificity rule in or "SPIN"].

Basic terminology

Probability that	K/as	Equals to
The test is +ve in diseased person	Sensitivity	TP rate
The test is -ve in diseased person	1 - Sensitivity	FN rate
The test is +ve in non diseased person	1 - Specificity	FP rate
The test is -ve in non diseased person	Specificity	TN rate

[Red box tests in diseased person , Green box test in healthy or non- diseased person]

PV (Predictive value)

- Probability of the person having the d/s when the test is +ve (PPV) or not having the d/s when the test is -ve (NPV).

Positive predictive value (PPV)

Indicates true positives out of total positives.

$$PPV = a / (a + b) = TP / (TP + FP)$$

$$= \frac{\text{Sensitivity} \times \text{Prevalence}}{\text{Sensitivity} \times \text{Prevalence} + (1 - \text{Specificity}) \times (1 - \text{prev.})}$$

Negative predictive value (NPV)

Indicates true negatives out of total negatives.

$$NPV = d / (c + d) = TN / (TN + FN)$$

$$= \frac{\text{Specificity} \times (1 - \text{prevalence})}{(1 - \text{sensitivity}) \times \text{prevalence} + \text{specificity} \times (1 - \text{prevalence})}$$

Likelyhood Ratio (LR)

- LR provides a direct estimate of how much a test will change the odds of having a d/s

$$LR = \frac{\text{Probability of result in diseased person}}{\text{Probability of result in non-diseased persons}}$$

Positive likelihood ratio (LR⁺)

Ratio b/w the probability of a positive test result given the presence of the disease and the probability of a

positive test result given the absence of the disease, i.e.

$$= TP \text{ rate} / FP \text{ rate}$$

$$= \text{Sensitivity} / (1 - \text{Specificity})$$

Negative likelihood ratio (LR⁻)

Ratio b/w the probability of a negative test result given the presence of the disease and the probability of a negative test result given the absence of the disease, i.e.

$$= FN \text{ rate} / TN \text{ rate}$$

$$= (1 - \text{Sensitivity}) / \text{Specificity}$$

Another useful formulae

$$\text{Sensitivity} \times \text{Prevalence} =$$

$$\frac{\text{No. who have D \& screened +ve} \times \text{No. who have D}}{\text{No. who have D} \times \text{Total number screened}}$$

[Source of the above formulae : www.mas.ncl.ac.uk/njnsn/medfac]

- Incidence = exposure rates of cases = $a / a + c$

- Incidence among non exposed (controls) = $b / b + d$

To summarize

Term	Equals to
PPV	True P/ total P
LR ⁺	TP/FP
NPV	True N/ total N
LR ⁻	FN/TN

Attributable Risk

$$AR = \frac{E - NE}{E} \times 100$$

$$\text{Relative risk (risk ratio)} = \frac{a}{(a + c)} \div \frac{b}{(b + d)} = \frac{E}{NE}$$

$$= \frac{\text{incidence of ds among exposed}}{\text{incidence of ds among non exposed}}$$

- Odds ratio (cross product ratio) = ad / bc

- Prevalence (prior probability) = $\frac{\text{All patients with ds}}{\text{all pt tested}}$

$$= \frac{(a + c)}{(a + b + c + d)}$$

Inherent Properties of a Screening test

Inherent properties of a screening test are --- Sensitivity, specificity, predictive accuracy.

Accuracy

- Also k/as validity of a test
- Accuracy is degree of closeness of a measured or calculated quantity to its actual (true) value
- Tests of accuracy are --- Mean chart, levy, shewhart control chart
- Accuracy or validity of a test *depends upon sensitivity, specificity & prevalence*

$$= (\text{Sensitivity}) (\text{Prevalence}) + [(\text{specificity}) (1 - \text{prevalence})]$$

$$= (\text{TP} + \text{TN}) / (\text{TP} + \text{FP} + \text{TN} + \text{FN})$$
- Predictive accuracy (predictive value) determines diagnostic power of the test.

Precision (reliability)

- Precision is degree of closeness of a measured or calculated quantity to its actual (true) value
- Precision is also k/as reliability, repeatability, reproducibility or consistency of a test
- Tests of precision are --- LJ charts, range chart, R- chart

- *Validity (accuracy) of a sensitive test is determined by --- Sensitivity & specificity.*
- *Reliability of a test is precision.*
- *PPV of a test is also k/as post-test probability of d/s or precision rate. PPV is the probability of having a disease in a positive test*
- *An ideal screening test should be 100% sensitive & 100% specific, but usually sensitivity may be increased at expense of specificity & vice-versa.*

Delphi Method

- Systematic interactive forecasting method
- A structural process for collecting and distilling knowledge from a panel of experts by means of a series of questionnaires interspersed with controlled opinion feedback.

Random Sampling Methods

Simple Random sampling

- Each and every unit of population has equal chance of being selected.
- Applied to small, homogenous, and readily available population.
- Methods used are lottery method, random number of tables, computer software

Systematic Random sampling

- Every kth unit of population is selected, where k is selected

by sampling interval.

- Sampling interval (K) = Total number of units in population / total number of units in sample

Stratified Random sampling

- Population is stratified into groups or classes in order to convert large non-homogenous population to homogenous subgroups, then random sample is drawn from selected groups or classes.

Cluster Random sampling (CRS)

- Study design effect model is used.
- When units of population are clusters or natural groups.
- This technique is used for immunization of children. In 30 x 7 WHO technique 30 clusters each containing 7 children of age group are immunized.

Multistage Random sampling

Multiphase Random sampling

Non-Random Sampling Methods

- Convenience sampling
- Quota sampling
- Snow- ball sampling
- Clinical trial sampling

The Kaplan-Meier estimator

The Kaplan-Meier estimator (also k/ as the product limit estimator) estimates the survival function from life-time data. In medical research, it might be used to measure the fraction of patients living for a certain amount of time after treatment. An economist might measure the length of time people remain unemployed after a job loss. An engineer might measure the time until failure of machine parts.

CORRELATIONAL TECHNIQUES

Correlation (r)

- Used to establish and quantify the strength and direction of the relationship b/w 2 variables. It indicates the degree of association b/w two variables or characteristics.
- Strength of relationship is indicated by the size of the coefficient (value), while its direction is indicated by the sign. A plus (+) sign means positive correlation.
- Correlation is represented by scatter diagram
- Value of correlation coefficient ranges from -1 to +1

$r = +1$ indicates a perfectly positive correlation (rise in one variable leads to proportionate rise in other) whereas

$r = -1$ indicates a perfectly negative correlation (rise in one variable leads to fall in other). Example: \uparrow in altitude is a/w \downarrow in no. mosquito.

$r = 0$ indicates there is no correlation (rise in one variable leads to proportionate no change in other).

Correlational coefficients are mainly 2 types :

1. **Pearson's product moment co-rrrelational coefficient**, used for ratio and interval scale data
2. **Spearman rank- order co-rrrelational coefficient**, used for ordinal scale data

A correlation b/w two variables does not necessarily demonstrate a causal relationship

Coefficient of Determination (r^2)

- Expressed as r^2
- Expresses the proportion of the variance in one variable by the variance in the another variable

Co-efficient of Variations

Unit free measure of dispersion .used to compare relative variability

$$CV = \frac{SD}{\text{mean}} \times 100 \text{ or } C.V. = \frac{\sigma}{\bar{X}} \times 100$$

CV is used to compare variability of 2 distribution.

- Association is simultaneous existence of 2 variables
- Correlation is relationship b/w 2 qualitative or continuous variables
- Regression provides structure (quantification) of relationship b/w 2 quantitative variables

Regression

- Regression is the change in measurments of a variable. It provodes structural relationship b/w 2 variables.
- If two variables are highly correlated, it then becomes possible to predict the value of one of them (dependent variable) from the value of other (the independent variable).

Types

Multivariate multiple regression Used for relationship b/w a set of quantitative variables

Multivariate logistic regression Used for relationship b/w

a set of qualitative variables

Regression co-efficient measure of change of one dependent variable with change in independent variable or variables (x_1, x_2, x_3, \dots)

Regression type	Subtype	Feature	Example
Linear	Simple	1 single continuous on single continuous variable	Age to BP
	Multiple	≥ 2 continuous (or categorical) independent variable to single continuous variable	Age ,sex,d/s on BP
Logistic	Simple	Single continuous (or categorical) independent variable to a single categorical variable	Smoking to lung cancer
	Multiple logistic	≥ 2 continuous (or categorical) independent variable on a single categorical variable	Relationship of multiple independent risk factors on occurence of d/s

SOME IMP. NEGATIVE POINTS

- Median is NOT important for ---Blood pressure.
- Bias can NOT be eliminated by or NOT a way of elimination of bias ---Multivariate analysis.

CLINICAL VIGNETTES

- A study was conducted to test role of herbal tea on prevention of common cold. Data was collected on the number of people who developed cold and those who did not developed cold and this data was tabulated in relation to whether they consumed herbal tea or not.

	Consumed herbal tea	Not consumed herbal tea
1. Had cold ---	12	23
2. Did not have a cold---	34	38

[AIPGME 2007]

A. Unpaired 't' test (Unpaired)

B. Paired 't' test

C. McNemae's chi-square test

D. Chi-square test

(Ans: D. Chi-square test)

- Amount of alcohol consumed by a group of people is recorded pre as well as post intervention programme. To assess the significant change in the amount of alcohol consumption appropriate statistical test is?

[AIPGME 2012]

A. Unpaired 't' test (Unpaired)

B. Paired 't' test

C. McNemae's chi-square test

D. Chi-square test

(Ans: B. Paired 't' test)

- A study who planned to find out the effect of iron supplementation during pregnancy on the birth weight of new born children. Two groups, one with iron supplementation and the other without iron supplementation during pregnancy were compared. Birth weight of newborns were recorded as mean + SD. Which significant test (statistical) is appropriate for comparison of birth weights between the two groups?

A. Unpaired 't' test

B. Paired 't' test

C. McNemae's chi-square test

D. Chi-square test

(MP 2008)

(Ans: A. Unpaired 't' test)

There are 3 important tests, questions are based upon

1. Chi-square test : For qualitative data
2. Student t test : For quantitative data when 2 samples are compared
 - Paired 't' test
 - Unpaired or independent 't' test
3. ANOVA test: For quantitative data when ≥ 2 samples are compared

If data are qualitative in nature, two type of tests are applied---

1. Chi-square (X^2) test

Applied when sample size is >30 . In the first qn data are 'had cold or did not have cold' are nominal and qualitative data. Chi square test (X^2) is the most important non parametric test used for testing hypothesis about nominal scale data (Used to compare percentage, proportions, and fractions in ≥ 2 different groups).

E.g. if 1/3rd of students in a class are stunted whereas in another class 1/3rd are underweight; test of significance to be applied is chi square test.

■ *McNemar's Chi-square test*

Is a variant of chi-square when paired data is used

■ *Fisher's exact test*

It is a variant of chi square test which is applied when sample size is < 30 .

2. Student 't' test

Applied when data are quantitative (parametric) in nature, data belong to interval scale

– *Paired 't' test*

Data are paired in a single group. Applied to compare means in paired data of independent observation from **one sample only**. E.g.

1. Recording of BP **before and after** giving drug to the same group of individuals.
2. Mean serum iron levels of anemia cases of group A before iron therapy and after iron therapy.

– *Unpaired 't' test* (or independent 't' test)

Applied to compare mean data of independent observation from two or more groups. E.g. To record effect of iron supplementation in A and B groups before and after giving drug to both groups

3. ANOVA test (ANalysis Of VAriance; F-test)

Mean birth weight of newborns in NICU -A is 2.5 kg, those of NICU-B is 2.4 kg and NICU-C is 2.6 kg.

Comparison of mean birthweights of NICU A,B,C is done by ANOVA test.

- A chest physician observed that the distribution of forced expiratory volume (FEV) in 300 smokers had a median value of 2.5 liters with the first and third quartiles being 1.5 and 4.5 liters respectively. Based on this data how many persons in the sample are expected to have a FEV between 1.5 and 4.5 liters?

A. 75

B. 150

C. 225

D. 300

[AIIMS Nov'05]

(Ans: B. 150)

In above case

Median = 2.5 L

First quartile = 1.5 L 3rd quartile = 4.5 L

So we can consider 2.5 as 150th value 75th value is 1.5 and 225th value is 4.5. No. of people b/n 1.5 and 4.5 L are expected $225 - 75 = 150$

- A diagnostic test for a particular disease has a sensitivity of 0.90 and a specificity of 0.80. A single test is applied to each subject in the population in which the diseased population is 30% what is the probability that a person, negative to this

test, has no disease?

- A. Less than 50% B. 70%
C. 95% D. 72% [AIIMS May' 06]

(Ans: C. 95%)

[Ans : Probability that the person with ve test results will not have disease is negative predictive value

1-sensitivity = probability of -ve test results in a pt with disease (false -ve)

Sensitivity = 0.9 means 90% of the diseased people screened by the test will give a "true positive result and the remaining 10% a FN result. Suppose total population is 100 diseased are 30 means $a+c = 30$

$$a/a+c = 0.9$$

$$d/b+d = 0.8$$

$$a+c = 30$$

So $a = .9 \times 30$	NPV	$= d/(c+d) \times 100$
$a = 27$		$= 56/(3+56) \times 100$
$c = 30-27=30$		$= .56/ 59 \times 100$
$= d = (b+d) \times 0.8$		$= 95\% \text{ aprox.}$
$= d = 70 \times 0.8 = 56$		

- In the pediatric ward of a hospital of 50 patients admitted on a day, 20 are girls and 30 are boys. Of the 20 girls 10 and of the 30 boys, 20 needed surgery. What is the probability that a patient picked up at random from that ward on that day would need surgery.

- A. 2/6 B. 3/5
C. 1/2 D. 6/25

[AIPGMEE' 2009]

(Ans: B. 3/5)

In the above mentioned qn probability of girls being picked up for surgery is 10 out of 50 = $10/50 = 1/5$

Probability of boys being picked up for surgery is 20 out of 50 = $20/50 = 2/5$

It is not like that, if a boy is being picked up for surgery, a girl will not be picked for surgery, so these events are mutually exclusive

For mutually exclusive events $P \text{ total} = P(A) + P(B)$

Probability of total patients being picked up for surgery will be $= 1/5 + 2/5 = 3/5$

■ Probability

- Probability is the chance of occurrence of an event
- Probability ranges from 0 to 1 i.e. it can not be less than zero or more than 1

• Probability rules :

Rules of addition :

For mutually exclusive events $P \text{ total}$

$$= P(A) + P(B)$$

Rules of multiplication:

For 2 or more independent events $P \text{ (total)} = P(A)$

$$P(B)$$

- A diagnostic test for a particular disease has a sensitivity of 0.90 and a specificity of 0.90. A single test is applied to each subject in the population in which the diseased population is 10%. What is the probability that a person positive to this test, has the disease?

- A. 90% B. 81%
C. 50% D. 91% [AIIMS Nov'05]

(Ans: C: 50%)

$$\begin{aligned} \text{PPV} &= [\text{prevalence} \times \text{sensitivity}] / [(\text{prevalence} \times \text{sensitivity}) - (1 - \text{sensitivity}) \times (1 - \text{specificity})] \\ &= [.1 \times .9] / [(1 \times .9) - (1 - .1) \times (1 - .9)] \\ &= .5 = 50\% \end{aligned}$$

- The 'p' value of a test comparing 2 drugs is 0.01, what is the inference?

- A. Probability of type II error is 1%
B. Power of test is 1
C. Probability, that drug A is better than drug B when in truth it, is not 1%
D. Probability, that drug B is better than drug A when in truth it, is not 1%

(AIIMS May'08)

(Ans. : C. Probability, that drug A is better than drug B when in truth it, is not 1%)

- In a population of 10000, 20% are affected by a disease. A test used for screening has 95% sensitivity and 80% specificity is applied. What would be the Positive Predictive Value?

- A. 54.3% B. 98.4%
C. 15.6% D. 45.3% [AIIMS Nov'09]

(Ans. 54.3%)

- You have diagnosed a patient clinically as having SLE and ordered 6 tests. Out of which 4 tests have come positive and 2 are negative. To determine the probability of SLE at this point, you need to know -

- A. Prior probability of SLE; sensitivity and specificity of each test
B. Incidence of SLE and predictive value of each test
C. Incidence and prevalence of SLE

D. Relative risk of SLE in patient

[AIPGMEE'05,'07 & 12, AIIMS May'06]

(Ans. A. Prior probability of SLE; sensitivity and specificity of each test)

PPV or post test probability of d/s or precision rate c/b derived by Baye's theorem.

$$PPV = \frac{(Sn \times Sp) \times 100}{[(Sn \times Prevalance) + \{(1-Sp)(1-Prevalance)\}]}$$

Pre test probability is prevalence. So its clear that to derive PPV one has to know Sn,Sp, and prior probability.

A. High validity and high reliability

B. Low validity and low reliability

C. High validity and low reliability

B. Low validity and high reliability

(Ans. B. Low validity and low reliability)

NOTES

- A new test for diabetes was carried out. Out of 80 people who were tested +ve, it was found that actually 40 had diabetes and out of 9920 people who were tested -ve, only 9840 do not have the d/s in actual. Sensitivity of the test is :

A. 50%

B. 33%

C. 66%

D. 75% [AIPGMEE'10]

(Ans. B. 33%)

TP are the cases who were found +ve for d/s and actually have d/s

TN are the cases who were found -ve for d/s and actually do not have d/s.

$$TP = 40$$

$$\text{Total negatives} = TN + FN$$

9840 were true negatives, so the FN were

$$9920 - 9840 = 80$$

Now applying in formula

$$\text{Sensitivity} = \frac{TP \times 100}{(TP + FN)}$$

$$= \frac{40 \times 100}{(40 + 80)} = 33\%$$

- Estimated mean hemoglobin of a sample of 100 women was found to be 10 mg% with a standard deviation of 1mg%. The standard error of estimate would be [AIPGMEE'12]

A. 0.1

B. 0.01

C. 0.001

D. 10

(Ans. A. 0.1)

- Using a new technique, Hb was estimated in a blood sample. The test was repeated for 10 times. The reports were: 9.5, 9.2, 9.4, 9.6, 9.7, 9.9, 10.2, 10.3, 10.5, and 12.1. Accurate value of Hb was estimated by standard tests to be 10.2. The new technique has [AIPGMEE'12]

GENERAL

Drugs used in medical - ectomies

Medical — ectomy	Drugs responsible for
• M~ Adrenalectomy	Mitotane, metyrapone (aminoglutethimide, KTZ, steroids also)
• M~ synovectomy	Yttrium (Y^{90}) and P^{32}
• M~ discectomy	Chymopapain (e.g. in ankylosing spondylitis)
• M~ prostatectomy/androgen ablation	LHRH agonist
• M~ castration (orchidectomy/oophorectomy)	GnRH analogues (e.g. Goserelin, buserelin, leuprolide)
• Pancreatectomy	Streptozocin, alloxan
• Curettage	High dose progesterones
• Medical menopause	Danazol

Some imp. Pseudo

- Pseudobronchiectasis is seen --- After pertussis (reversible if a/w collapse.)
- Pseudodementia --- Endogenous depression
- Pseudochylous ascites --- Malignant ascites
- Pseudochylous pleural effusion --- TB + RA
- Pseudo-lymphoma is seen in --- **Sjögren syndrome**
- Pseudo paralysis --- In Hypokalemia, scurvy, septic arthritis, RA, cong. syphilis, trichinosis, osteomyelitis

[Mn: ESCORTS]

- Pseudo bubo --- In **Donovanosis**
- Pseudopapillitis --- In **Hypermetropia**
- Pseudoclaudication --- *Intermittent claudication d/to compression of cauda equina.*
- Pseudohyperkalemia --- Secondary to iatrogenic hemolysis of RBCs.
- Pseudoachalasia --- Adenocarcinoma of cardia
- Pseudohyponatremia --- Hyponatremia with a normal osmotic pressure (as in hypertriglyceridemia and hyperagammaglobulinemia).
- Pseudoporphyria --- Seen with *naproxen* use in JRA

Most Common Complication of.....

	In Children	In Adult
• Measles	ASOM	Bronchopneumonia
• Mumps	Aseptic meningitis	Orchitis, oophoritis
• Rubella	Arthralgia	
• Chickenpox	CNS Complications (ataxia)	Interstitial pneumonia secondary bacterial infections of skin
• Meningococcal meningitis	Water-house-Fredrickson syndrome	
• Pertussis	Pneumonia	Bronchopneumonia

Not a complication of..... / --- rarely causes

- Measles --- Aseptic meningitis, optic neuritis, pancreatitis, cataract
- Mumps --- Pneumonia, appendicitis
- Chickenpox --- Enteritis, pancreatitis
- Diphtheria --- Vertigo
- Pertussis --- Myocarditis, bacterial endocarditis
- Pneumonia --- Amyloidosis

→ *Disseminated gonococcal infection does not cause — Nephritis*→ *Botulism, staphylococcal food poisoning does not cause — Fever, diarrhoea*→ *Serum amylase is not increased in — Acute appendicitis*

Organs not affected in

- IUGR — Brain (lung, heart least affected)
- Maternal DM — Brain, kidney, tongue (no macroglossia)
- Sarcoidosis — Adrenals (least affected)
- TB — Heart, pancreas, skeletal muscle.
- Cryptococcosis — Kidney (rarely affected)

→ *Amyloidosis does not occur in carcinoma bronchus, pneumonia*→ *Clubbing does not occur in Chronic Bronchitis, SCLC, Bronchial asthma, primary pulmonary HTN*

Hemodialysis is –

Useful in...	Useless / Contraindicated in
Barbiturates poisoning	BZD/Diazepam toxicity (d/to high PPB)
Ethanol, Methanol	Propanolol (d/to large volume of distribution)
Chloral hydrate	Kerosene poisoning
Salicylate	Morphine
Theophylline	Opium
Ethylene glycol	Organophosphorus poisoning
Lithium	Digoxin (Large volume of distribution)
	[Mnemonic : Birthday Party Ka Mood]

Hemo perfusion

Is considered in severe poisoning d/to chloramphenicol, disopyramide, and hypnotic sedatives, phenytoin procainamide and theophylline. [CP₂DT]

Causes of

Miosis / Constricted/ Small pupil	Mydriasis (Dilated Pupil)
Old age (MC cause)	Anxiety (MC cause)
Horner syndrome	Childhood
ARP	Adie's pupil
Barbiturates, BZD	Amphetamines, cocaine
Pontine hemorrhage	Cerebral death
Opiates (Heroin, morphine)	Psychedelics (LSD & Phencyclidine)
Sympathetic paralysis	Parasympathetic paralysis
Metabolic encephalopathy (Small reactive)	
[Mnemonic : B.M. Shampoo]	[Mnemonic : A ₃ C ₃ P ₃]

CLUBBING

- Clubbing may occur in isolation or may be the earliest manifestation of hypertrophic osteoarthropathy (HOA), which in its later stages is c/by periosteal new bone formation and synovitis.
- Clubbing is caused by the proliferation of connective tissue in the nail bed and volar pad of the digits.

Imp. causes :

- 1. Pulmonary:** bronchogenic / pleural neoplasms, lung abscess, empyema, bronchiectasis, interstitial pneumonitis (chronic), CF, sarcoidosis, pulmonary AVMs including hepatopulmonary syndrome, benign asbestos-related pleural lesions.
- 2. GI:** IBD, sprue; cancer of the esophagus, liver or bowel; cirrhosis; amebic dysentery.
- 3. CVS :** Cyanotic CHD, SBE
- 4. Others -** hyperthyroidism ("thyroid acropachy"), HIV

Unilateral clubbing may be seen in :

- AV fistula, aneurysm of subclavian a.
- Bronchogenic Ca
- Cervical rib
- Pancoast tumour

Clubbing seen in lower extremities only :

- Aortic aneurysm
- PDA

→ Clubbing is rare in chronic bronchitis, COPD if a/w an intrathoracic malignancy, bronchiectasis

→ Clubbing does not occur in pure emphysema, asthma and primary pulmonary hypertension.

Transudate and Exudate

- Transudate** is filtrate of plasma without change in permeability (similar to blood plasma). Seen in early stage of inflammation due to vasodilatation
- Exudate** is inflammatory edema fluid seen in later stages of inflammation d/to ↑ permeability.

	Transudate	Exudate
Colour	Clear, serous	Cloudy, tan
WBC count	< 1000/ mm ³	> 10,000/ mm ³
RBC count	< 10,000/mm ³	> 10,000/ mm ³
Proteins	< 3.0 g/dl	> 3.0 g/dl
Sp.gravity	< 1.016	> 1.016
Glucose	Normal	Low
LDH	Normal	> 67 %
Cells	Few cells (mainly mesothelial), bacteria -nt	Many cells (inflammatory & parenchymal), bacteria +nt

- Specific gravity
 - in edema/ascites fluid → <1.012 (in transudate)
 - >1.020 (in exudate)
- In effusion fluid → <1.016 (in transudate)
- >1.016 (in Exsudate)
- In Hydatid fluid → 1.005-1.009
- Of Urine → 1.015-1.025
- Hallmark of an exudative fluid are --- Proteins >50% of serum level (3.0 g/dl), LDH >2/3rd of serum level.

Ascitic Fluid

Transudative Ascites	Exudative Ascites
<ul style="list-style-type: none"> ○ Occult cirrhosis ○ Rt sided venous HTN, portal HTN ○ Hypoalbuminemic states <ul style="list-style-type: none"> - Nephrotic syndrome - Protein losing enteropathy 	<ul style="list-style-type: none"> ○ Peritonitis ○ Tubercular peritonitis ○ Pancreatic ascites (often) ○ Malignancy & infection

- In tubercular peritonitis ascitic fluid changes from transudate to exudate.
 - Mucinous ascites is characteristically seen in pseudomyxoma peritonei (rupture of mucocoele of appendix, a mucinous ovarian cysts, mucin secreting intestinal/ovarian adeno Ca) and rarely in colloid Ca of stomach/colon
 - Ascites d/to portal hypertension can be diagnosed with 95% certainty by calculating SAAG i.e. serum ascitic albumin gradient. Value >1.1 is indicative of portal hypertension as cause of ascites.
- (SAAG = Serum albumin concⁿ - ascites albumin concⁿ)

Pleural Effusion

Transudative Effusion	Exudative Effusion
(D/to ↑ hydrostatic pressure) <ul style="list-style-type: none"> ○ CHF is the m/c cause ○ <u>Nephrotic syndrome</u> ○ Cirrhosis ○ Hypoprotecinemia ○ Myxedema ○ Peritoneal dialysis 	<ul style="list-style-type: none"> ○ M/c cause is <u>parapneumonic</u> effusion d/to bacterial pneumonias, lung abscess, bronchiectasis ○ Pulmonary Embolism ○ Malignancy ○ Traumatic (Perforation, Sx) ○ Collagen vascular disorders (RA, SLE)

- Mixed pleural effusion is seen in myxedema, pulmonary emboli, pericardial d/s, sarcoidosis, amyloidosis.

- Overall m/c cause of pleural effusion is CHF.
- M/c cause of exudative pleural effusion in developing countries is TB.
- Low glucose exudative pleural effusion
 - Bacterial infections, empyema
 - Malignancy
 - RA
 - Hemothorax
- Increase amylase in exudative pleural effusion
 - Esophageal rupture
 - Pancreatitis
 - Malignancy
- Chylous pleural effusion → in thoracic duct obstruction
- In RA → Pleural & pericardial effusions are an exudate with ↓ complement, low glucose and high level of cholesterol
- Pleural effusion with cholesterol crystals is seen in
 - Hypothyroidism
 - TB
 - RA

Transcellular Fluid

- Portion of total body water contained within epithelial lined spaces.
- It is the smallest component of ECF, which also includes interstitial fluid and plasma. It is about 2.5% (1 Litre) of the total body water.
- Examples of this fluid are CSF, ocular fluid, joint fluid, & sweat, digestive secretions, pleural fluid.

CNS

TREMORS

- Resting (static) tremor — In Parkinson's disease
- Intention tremor — In cerebellar lesion
- Postural tremor — In Thyrotoxicosis (exaggerated physiological tremors), essential familial tremor
- Flapping tremor / Asterixis — In Hepatic encephalopathy, renal failure, resp. failure, metabolic encephalopathy.
- Perioral tremor — General paresis of insane

- Perioral movements in rabbit syndrome are part of tardive dyskinesia which is a long term side effect of antipsychotics.

ABNORMAL GAIT

- Circumduction / Hemiplegic gait — In hemiparesis
- Stamping (Tabetic gait), slapping gait — In post column lesion (tabes dorsalis) & SADC.
- Spastic gait — In UMN lesions
- Ataxic gait — In cerebellar lesion
- Apraxic gait — In frontal lobe d/s usually accompanied by dementia
- Waddling gait — In prox^m muscle weakness of LL, Muscle dystrophy or CDH
- Equinus / High Steppage gait — In foot drop (Peroneal muscle dystrophy / neuropathy)
- Shuffling / Festooned gait — In Parkinsonism
- Festinant gait — In Parkinsonism, CO poisoning, Old age, ankylosing spondylitis
- Astasia-abasia — hysterical gait

→ Positive Romberg's sign is seen in sensory ataxia (which may be d/to posterior column lesion, vestibular lesion, SADC etc.)

→ Lower quadrantanopia is seen in parietal lobe lesion

→ Upper quadrantanopia is seen in ---Temporal lobe lesion

→ In parietal cortex lesions proprioception & fine touch are most affected and pain is the least (order of affection : proprioception & fine touch > temp > pain)

→ Complex hallucinations (of smell, sound, vision, memory) are seen in temporal lobe lesion.

→ Frontal release signs (eg. thumbs sucking & appearance of other primitive reflexes) are seen in Frontal lobe lesion.

→ Stimulation of area premotor cortex 6, 8 (frontal eye field) causes — saccadic eye movt. (but no hallucination)

Stimulation of area 19 (occipital eye field) causes — saccadic eye Movt. + visual hallucination

→ Visual cortex is s/by — posterior cerebral artery (mainly) + MCA

Cerebral achromatopsia

Colour blindness d/to B/L strokes involving ventral portion of occipital lobe. Perceives only shades of grey. Prosopagnosia is usually associated with it.

Colour Anomia

Patient discriminate colour but can not name them d/to infarction of dominant occipital lobe.

Dressing apraxia

Lesion of non-dominant parietal lobe

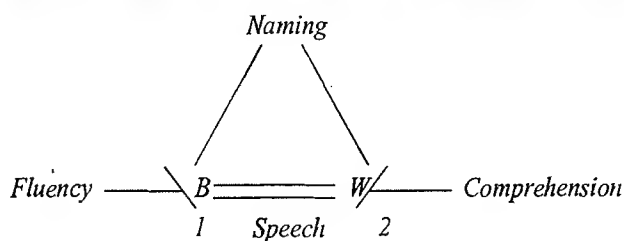
Prosopagnosia

Inability to recognize faces

d/to lesion of non-dominant temporal lobe (acc. to ganong) or fusiform/ lingual gyri of occipito temporal lobe B/L lesion (acc. to harrison) perisylvian and insular cortex due to occlusion of superior division of the MCA.

Aphasia

	Broca's Aphasia	Wernicke's Aphasia
Speech	Telegraphic & quite informative	Voluminous but uninformative
1 Comprehension	Preserved	Impaired
2 Repetition of spoken language	Impaired	Impaired
3 Naming	Impaired	Impaired
4 Fluency	↓se	↑se or preserved
5 Insight	Present	Absent
6 Other/f	Agrammatism	Jargon Aphasia, neologism
7 Site of lesion	Inferior frontal gyrus (Emboli in superior division of MCA)	Sup. temporal gyrus/ Inferior parietal strip (Emboli in inferior division of MCA)



Above diagram is an easy way to remember [Mnemonic: British Council WelFare BCWF = In B 'C' is preserved]

Speech has 4 components: Comprehension, fluency, naming, repetition.

◦ In Broca's aphasia (1) fluency is ↓, there is impaired naming, repetition. Comprehension preserved.

◦ In Wernicke's aphasia (2) comprehension is lost and there is impaired naming, repetition.

◦ Anomic aphasia, also k/as dysnomia, nominal aphasia, and amnesic aphasia; is a severe problem with recalling words or names. The lesion is often temporal parietal area. The angular gyrus may also be affected, causing alexia and agraphia.

Anatomical & Functional Cortical Areas

Lobe	Location	Area (Area No.)	Function	Lesion
1. Frontal	Precentral gyrus	Motor area (4)	Controls voluntary motor activities	Cont/L Hemiparesis (UMN type), Monoplegia (single limb paralysis)
		Premotor area (6)	Control EPS	
		Frontal eye field (6,8)	Responsible for voluntary eye movt.	Deviation of eye towards the side of lesion (Saccadic movts. of eye)
	Inferior frontal gyrus	Motor speech area (44, 45) (Broca's area)	Controls spoken speech (Language)	Motor (Broca's/ expressive) aphasia
		Prefrontal cortex (9,10,11,12)	Emotional control Social behavior	Lack of initiation Antisocial behavior
2. Parietal	Post central gyrus	Somato- sensory area / Primary somesthetic area S-I (3, 1, 2)	Highest area for general conscious Sense perception (touch, pain, temp)	Defect in sensory perception & processing to S-II
	Sylvian fissure	S-II	Learning based on tactile discrimination, Sensory speech	Sensory aphasia (will produce difficulty in learning in blinds)
	Posterior part of parietal lobe	Somato sensory association area (5,7)	Synthesis of senses (formed sense) Maintenance of body image, constructional skills, Spatial orientation	Tactile agnosia (astereognosis) Neglect of opp. half of body (constructional apraxia, dressing apraxia)
3. Temporal	Gyrus of Heschl in floor of lat. sulcus	Audiotensory area (41,42)	Auditory perception (Sound is heard)	Impaired hearing (deafness if B/L extensive Lesion)
	Sup. temporal gyrus	Auditopsychic area (22)	Sound is 'interpreted' Smell balance	Auditory agnosia , impaired non-verbal memory, Wernicke's aphasia , complex auditory & olfactory hallucinations.
4. Occipital	Post calcarine sulcus	Visuosensory area (17) (striate area)	Highest area for perception of visual sense	<i>Homonymous hemianopia with macular sparing</i> (because macular area has largest representation)
	Surrounds the area 17	Visuopsychic area (18,19) (Parastriate/peristriate area)	Correlation of visual impulses with past memory & recognition of object seen & also the depth.	Visual agnosia

ALEXIA & AGRAPHIA

- Lesions of the angular gyrus are a/w alexia & agraphia.

Finding	Seen in lesion of
1. Alexia + sensory aphasia	Dominant post. lobe
2. Alexia + agraphia	Angular gyrus
3. Alexia (pure agnosic)	Splenium of corpus callosum

IMP. POINTS

- Frontal lobe lesions are a/w jacksonian march & continuous partial seizures.
- Temporal lobe lesions are a/w **complex auditory and gustatory hallucinations** with olfactory aura. Complex hallucinations of smell, taste, vision, memory are present. Also seen in temporal lobe epilepsy.
- Monoplegia (single limb paralysis) is seen in lesions of motor area 4.

MONOPLLEGIA

- Monoplegia (19% of strokes) usually indicates small infarcts of the **motor cortex (area 4)** or centrum semiovale.
- Lesions of medial portion of precentral gyrus cause predominantly distal leg weakness.
- Lesions of medial part of the premotor cortex and supplementary motor area cause contralateral hemiparesis, more prominent in the leg, and predominating proximally in both arm and leg.
- Monoplegia caused by capsular and brainstem strokes → Weakness equally distributed proximally and distally and suggests a somatotopic organization of the pyramidal tracts:

Spastic Paraplegia is seen in

- Tropical spastic paraparesis d/to HTLV-1 infection
- Toxins (Lathyrism, cassava)
- Multiple sclerosis
- Tropical spastic paraparesis d/to HTLV-1 infection
- Amyotrophic lateral sclerosis
- Spinal injury, herniation of thoracic disc
- Spastic CP.

MOTOR NEURON LESIONS

- UMN's are divided into flexor and extensor biased UMN's.

- Corticospinal tracts and rubrospinal tracts (upper limbs) are flexor biased
- Reticulospinal and vestibulo-spinal tracts are extensor biased.

- Therefore lesions involving UMN tracts above the midbrain result in *decorticate rigidity* [extension of lower limbs and flexion of upper limbs (as rubrospinal tract remains intact). DTR are normal.
- Transection of the brainstem at or below midbrain level (below red nucleus and above vestibular nuclei) results in *decerebrate rigidity* d/to unopposed extensor biased UMN's. There is extensor rigidity or posturing in both upper and lower limbs. extensor rigidity is γ -loop dependent. Section the dorsal roots interrupts the γ -loop, and the rigidity is relieved

Drugs in Various Seizures

	DOC (1st line)	Drugs not to be given
Partial Seizures (simple/complex)	Carbamazepine, phenytoin	
Generalized seizures/GTCS	Valproate, lamotrigine, topiramate	Ethosuximide
Absence/petit mal seizures	Valproate, Ethosuximide	Phenytoin
Neonatal seizures	Phenobarb	
Myoclonic seizures/ Atonic seizures	Valproic acid (clonazepam is alternative) lamotrigene, topiramate	

- *Ix* : Video EEG is diagnostic for epilepsy/seizure disorder
- Myoclonic seizures are seen in ---SSPE
- Carbamazepine is the DOC for simple partial seizures, complex partial seizures, psychomotor epilepsy
- Naloxone is useful for t/t of opioid induced seizures
- Drugs useful in status epilepticus are --- I.V. lorazepam is the DOC (I.V. diazepam is alternative), phenytoin, fosphenytoin, phenobarb, and in refractory cases GA like propofol, pentothal sodium, midazolam
(Carbamazepine is ineffective)
- Clonazepam is NOT used in ---GTCS

PARKINSON'S DISEASE (PD)

- Extrapramidal disorder char/by triad of
Rigidity + bradykinesia + resting tremors.
Resting tremors are earliest symptom.
- Characteristic **Resting tremors** of 4-6 Hz frequency (cycles/ sec.) are seen
- Postural tremors are of 8-10 Hz, persist on movement.
- D/to lesions of substantia nigra.
- DTRs are normal but postural reflexes are NOT preserved.
- Flexor plantar response (Negative babinski)
- Masked/ expressionless facies
- Drug induced parkinsonism
M/c caused by phenothiazines. T/t is by central anticholinergics like benzhexol (trihexyphenydol)
- Most preferred site for deep brain stimulation in Parkinson's d/s → Subthalamic nucleus.

ALZHEIMER'S DISEASE (AD)

- M/c cause of dementia.
- Presents with subtle onset of memory loss f/by slowly progressive dementia that has course for several years (irreversible & degenerative dementia).
- Some patients are unaware of their problem (anosognosia). Hallucination and delusions are common. Sleep wake pattern may be disturbed.
- CA3 and CA1 neurons of hippocampus and entorhinal/ temporal cortex are damaged. Amygdala, brainstem are also involved. Cerebellar neurons are resistant to AD related damage. Agnosia is usually not seen.
- **Pathology**
Gross /diffuse atrophy of cerebral cortex a/w secondary enlargement of ventricular system.
- **Microscopy**
 - 1.Extracellular micro-senile neuritic plaques made up of A β amyloid, apoE.
 - 2.Silver staining **neuro fibrillary tangles** in cytoplasm that represent abnormally phosphorylated tau (τ) protein
 - 3.Accumulaⁿ of A β amyloid in arterioles (*amyloid angiopathy*)
- **Risk factors**
Old age is the most important risk factor. Other risk factors are +ve family history, female gender, past h/o head trauma, lower educational attainment, and **Down's syndrome**.
- **T/t:**
Tacrine (cholinesterase inhibitor), Velnacrine, Rivastigmine, Donepezil & Galantamine

- *Earliest metabolic changes in AD occur in parietal cortex (& in temporal lobe, entorhinal cortex)*
- *AD is a/w ↓ level of Ach . Choline Acetyl transferase & nicotinic cholinergic receptors in cerebral cortex.*
- *In AD there is degeneration of cholinergic neurons in nucleus basalis of Meynert and reduction in NE levels in brainstem nuclei such as locus coeruleus.*
- *Protein misfolding is seen in → Alzheimer's d/s, BSE, cystic fibrosis.*
- *Age related dementia or Alzheimer's d/s is a/w ↑ed levels of homocystine.*
- *Dopamine is found to be significantly depleted in the brain of Parkinson's disease (PD) patients and Ach in Alzheimer's disease (AD) patients.*

Pick's d/s

- Progressive dementia
- Atrophy of frontal and temporal lobes
- Pick bodies

MID (Multi infarct Dementia)

- Multiple strokes
- Cerebral amyloid angiopathy is a risk factor
- Risk factors – HTN, DM, CAD

Diffuse Lewy body d/s

- Found in substantia nigra in Parkinson's ds
- 2nd m/c cause of degenerative dementia after AD
- Fluctuation of behavior, delusions, visual hallucination
- Occipital lobe involved.

HUNTINGTON'S DISEASE (HD)

- Autosomal dominant disorder. Gene is located on chromosome 4 . A/w CAG trinucleotide repeat.
- The symptoms of the d/s are caused by a significant reduction (volume and activity) of two principal neurotransmitters namely **Acetylcholine** and **GABA**, in turn affecting the activity of the Dopamine, which becomes hyperactive.
- Juvenile form (> 80 CAG repeat) : Chorea is characteristic.
- Adult HD (> 60 CAG repeat): No chorea but dementia present.
- Preferential loss of small to medium neurons preferably GABA sparing type.
- DOC is haloperidol.

Meningoencephalitis

- Meningoencephalitis with b/L frontal and temporal lobe involvement is d/to HSV.
- MRI shows only meningeal enhancement in meningitis while in HSV encephalitis on T2 weighted and FLAIR MRI show high intensity lesions in orbitofrontal, anterior and medial temporal lobes in most patient within 48 hr of onset of symptoms.

ADEM

(Acute Disseminated EncephaloMyelitis)

- Acute onset of polyfocal CNS deficits.
- Seen in neuromyelitis optica & multiple sclerosis.
- T/t : i/v Methylprednisolone.

GBS (Guillain - Barré syndrome)

- Also k/as post infectious polyradiculoneuropathy or acute segmental demyelinating polyradiculoneuropathy (motor >> sensory loss; vibration and proprioception). Sensory neuropathy may be present at the onset
- Begins 5-21 days after infections (e.g. Campylobacter jejuni), vaccines (measles) etc.
- M/s weakness is relatively symmetrical, usually proximal, begins in legs & progress to arms (ascending) mild distal sensory loss.
- Areflexia (DTR lost), sphincters are spared
- Lab/f - ↑ in CSF protein without ↑ in cells (no pleocytosis). Albumino-cytologic dissociation
- *Cause of death* : dysphagia and facial weakness are impending signs of respiratory failure.

Fisher variant of GBS/ Miller-Fisher Syndrome

- Characterized by triad of
Acute external ophthalmoplegia + Ataxia + Areflexia
3'A' (Features simulate SACS of spinal cord)
- Adults and children both c/b affected & generally fully recovered
- Anti-GQ 1b antibodies
- Demyelinating pattern on EMG

- Bickerstaff's encephalitis is characterized by triad of --- Acute external ophthalmoplegia + Ataxia + Lower CN palsy
- GBS is also k/ as acute idiopathic polyradiculoneuropathy (AIDP).
- Pattern of weakness in GBS is known as Landry ascending paralysis (symmetrical motor weakness usually ascending).
- Chronic inflammatory demyelinating polyneuropathy (CIDP) is chronic variety of GBS — severe weakness with flaccid tetraplegia. c/by onion bulb appearance on biopsy (d/ to imbricated layers of attenuated Schwann cell processes surrounding axons)
- Congenital GBS : rare, generalized hypotonia, weakness and areflexia in neonate.

Amyotrophic Lateral sclerosis (ALS or Lou Gehrig's ds)

- M/c form of progressive neuron disease.
- Both UMN & LMN (AHC of spinal cord) are affected.
- In 40% individual there is *mutation in gene for super oxide dismutase (SOD)*
- Loss of fibres in lateral column, fibrillary gliosis, spheroids in proximal axons (accumulation of neurofilaments).
- C/I/f
 - No CN involvement (rarely 12th CN may be involved) although pseudobulbar and bulbar variants exist.
 - No bowel / bladder involvement
 - No ocular muscle involvement
 - No sensory change, no pain
 - Normal X-ray spine
- Spasticity is late sign (with involvement of CST), ↑ DTR
- In proximal motor axons spheroids present (accumulation of neuro filament)
- Degeneration of cholinergic motor neurons in the brainstem & spinal cord are a/w one form of - ALS
- R_x: no T/t available, although Riluzole increase survival modestly.

FRIEDRICH's ATAXIA

- M/c familial ataxia with AR inheritance (gene is located on chromosome 9q13)
- Presents in 1st or 2nd decade (onset < 10 yr)
- Degeneration of 3 long spinal tracts occurs:
 1. *Spinocerebellar(or Pyramidal) tract* → Ataxia, dysarthria (slurred speech), Areflexia (Loss of ankle jerk, absent DTRs, and nystagmus).
 2. *Lateral CST (dorsal tract)* → leads to extensor plantar
 3. *Posterior columns* → lead to frequent falling (staggering gait, +ve Romberg's sign, loss of position/ vibration sense)

- Ataxia is slowly progressive (progressive spinocerebellar degeneration) & involves LL > UL
- Intelligence is preserved
- A/w Type I DM, Vit E deficiency
- Other features
 - Large heart (HCM) → CCF → death
 - Pes cavus & Kyphoscoliosis, hammer toes
 - Optic atrophy
- **Frataxin** protein is involved. Trinucleotide repeat is GAA.

Sub acute combined Degeneration (SACD)

- Diffuse myelopathy of spinal cord d/to long standing vitamin B₁₂ deficiency, which impairs function of methionine synthetase & methyl malonyl Co A mutase.
- Paresthesias in hands & feet are earliest sign (Pins & needles feeling)
- Demyelination + gliosis (astrocytic) occur initially in *posterior columns* (of lower cervical & upper thoracic region) - spreads up & down - later involvement of *lateral column* (combined degeneration)
- Early loss of vibration & position sense (more in legs) & progressive spastic & ataxic weakness, reflexes increase initially, later loss of reflexes d/to super imposed neuropathy
- Optic atrophy, irritability, dementia may present later (*Megaloblastic madness*)
- No focal spinal cord level
- D/g : low serum vit B₁₂ level & +ve schilling test
- R_x : vit B₁₂ (cobalamin)

- Extensor plantar is seen in ---Friedreich's ataxia, SACD
- Extensor plantar (positive Babinski sign) + Loss of DTR (ankle jerk) is a feature of both Friedreich's ataxia > SACD.
- Extensor plantar with preserved sensations ---SACD
- Examples of white matter disease are --- multiple sclerosis, acute disseminated encephalomyelitis, GBS, Friedreich's Ataxia etc.

Myotonia dystrophica

- M/c type of muscle dystrophy in adults
- AD inheritance. Transmitted by mutation in gene 19q which leads trinucleotide repeat
- Myopathy is typically **distal**. Usually appears by age of 5 years & causes slow relaxation of hand grip following a

forced voluntary closure.

- Frontal baldness, temporalis and masseter atrophy are seen. Other cl/f include gonadal atrophy, cardiomegaly, foot drop, wrist drop, difficulty in swallowing

D/d of Fedrich's ataxia, Tabes Dorsalis, SACD

Feature	Fedrich's ataxia	Tabes Dorsalis	SACD
1. Tract involved	Long tract degenera ⁿ - Pyramidal - Dorsal - Spino-cerebellar	Posterior column, DRG, Nerve roots	Posterior columns, pyramidal tract, peripheral nerves
2. Cause	Mutation of frataxin gene at chr13, AR	Chronic progressive demyelination	
3. Reflexes	Areflexia in LL	Absent at patella, achilles tendon	+ (Lost in late stages)
4. Babinski's sign (Extensor plantar)	+	-	+
5. Joint position, vibration sense	Lost	Lost	Lost
6. Pain, temp	Intact	Intact	Intact
7. Other Cl/f	Wide based ataxia, nystagmus, dysarthria, dysmetria	Anisocoria, Argyll robertson's pupil, Lightening pain in legs	Progressive spastic weakness & ataxia
7. Associated anomalies	CMP, optic atrophy, DM	Bladder disturbances.	Low serum B ₁₂ , Megaloblastic/pernicious anemia

Multiple Sclerosis

- Demyelinating white matter d/s.
- MRI will show lesions in the white matter.
- Fresh brain sections show demyelinating brown plaques around the occipital horn of lateral ventricle in white matter.
- Activity of M- is assessed by pleocytosis, enhancing CT-lesion
- Cl/f -- Acute optic neuritis.
- Oligoclonal bands in CSF gel electrophoresis are seen in >85% of patients.
- MRI is IOC & is diagnostic.

On Gd MRI T2 weighted (spin -echo) image --- Residual MS plaque remains visible indefinitely as a focal area of hyperintensity. 1/3 rd of T2 weighted lesions appear hypointense (black holes) on T1 weighted imaging. These black holes may be marker of demyelination and axonal loss.

- **Charcot's triad** of dysarthria (scanning speech), nystagmus, and intention tremors indicates involvement of the cerebellum.
- *Uhthoff phenomena* is seen in MS & optic neuritis. Worsening of neurological symptoms when body gets heated from hot water.

→ *Wyburn-Mason syndrome* is a/w mesencephalo-oculo-facial angiomas.

→ *Hallewörden-Spatz d/s* is due to cysteine accumulation. C/by triad of gliosis in the globus pallidus + iron deficiency anemia + axonal spheroids. Eye of the tiger sign + Dioxygenase deficiency in the globus pallidus is +nt.

→ *Neuromyelitis optica (Dawson's disease)* is a variant of multiple sclerosis.

NEUROCUTANEOUS DISORDERS/SYNDROMES

Neurocutaneous Disorders include

1. Neurofibromatosis I & II.
2. Tuberous Sclerosis.
3. Von Hippel Lindau (VHL) disease.
4. Sturge Weber Syndrome.

Other rare entities are

5. Klippel-Trenaunay-Weber Syndrome
6. Osler-Weber-Rendu Syndrome
7. Wyburn-Mason Syndrome
8. Linear Sebaceous Nevus Syndrome
9. Neurocutaneous Melanosis
10. Waardenburg Syndrome Type 1 & 2
11. Fabry's Disease

Neurofibromatosis (NF -I & II)

- Chromosome 17q (NF-1) and 22q (NF-2) involved.
- NF-1 is also called Von Recklinghausen d/s. Criteria for the diagnosis of NF1 ≥ 2
 - (a) ≥ 6 Cafe'-au-lait spots macules
 - (b) ≥ 2 Plexiform neurofibroma.
 - (c) Freckling in the axillary or inguinal region
 - (d) Optic glioma
 - (e) Lisch nodules (iris hamartomas)

(f) A distinctive osseous lesion such as sphenoid dysplasia or thinning of long bone cortex with or without pseudarthrosis

A first degree relative with NF--1 by the above criteria

- Ventriculomegaly, macrocephaly & short stature may be seen.

VHL Syndrome

- Triad of multiple renal cysts + retinal angiomas + craniospinal hemangioblastomas.
- Patients are prone to RCC (may be b/L), pheochromocytoma, pancreatic tumours and endolymphatic sac tumour.
- Neurocutaneous syndrome.

Tuberous Sclerosis

- Also k/as **Koenen's tumour**.
- AD disorder
- **Vogt triad** : Seizures + MR (mental retardation) + angiofibroma seen in tuberous sclerosis.
- Adenoma sebaceum/Facial angioma (75 %)
- Skin: Hypomelanotic macules in 90 %, "Confetti" hypopigmented skin lesions. Ash leaf spots, Shagreen patch.
- Other : Ungual fibroma (15 to 20 %), Forehead plaque
- Heart : Rhabdomyosarcoma.

Sturge - Weber's Synd

- Hemiatrophy of cortex
- Capillary Hemangioma in distribuⁿ of 5th nv, involving upper face/leptomeninges/choroid
- *Gyriform/snail track/tramline calcification* on skull X-ray in parieto-occipital region
- Ipsi/L glaucoma with cont/L homonymous hemianopia, hemiparesis & hemisensory disturbances
- **Port-wine stain**.

NEUROPATHIES, PARALYSIS

Dying Back Neuropathy

- Neuropathy a/w retrograde axonal degeneration
- Seen with
 1. Toxins (arsenic)
 2. DM
 3. Porphyria

Demyelinating Neuropathy

Nerve conduction velocity (NCV) is ↓ ed.

- Charcot-Marie-tooth-1 d/s is the m/c hereditary cause
- AIDP: Acute inflammatory demyelinating polyradiculopathy is seen in GBS
- CIDP: Chronic inflammatory demyelinating polyradiculopathy is seen in HIV
- HSMN (Hereditary sensory motor neuropathy)
- HNPP
- MMN (Multifocal motor neuropathy)

→ Descending paralysis is classically seen in botulism and diphtheria.

→ Leprosy is an axonal neuropathy, so conduction velocity is normal.

→ Sensory neuropathy is seen in HIV

→ Predominant motor neuropathy are seen in --- Prophyria (M or SM), GBS (M, SM) & Lead (M > S or M)

Amyotrophic lateral sclerosis, poliomyelitis, and Nm junction disorders.

→ Inverted champagne bottle appearance of lower limbs is seen in Sensory-motor neuropathy causing distal muscular atrophy

& Charcot-Marie-Tooth d/s, peroneal m/s atrophy

Neuropathy by Fibre type

Type	Example
Small-fibre sensory (Painful neuropathy with dissociative sensory loss)	HSN, LL (Lepraematous leprosy), DM, Amyloidosis, Tangier d/s, Fabry's Dys-autonomia (Riley Day syndrome), HIV & ART related neuropathy
Large-fibre sensory (Ataxic neuropathy)	Sjogren's, B ₁₂ deficiency, Friedrich's ataxia, Cisplatin, pyridoxine
Motor predominant	Acute GBS, HSMN, AIP, Diphtheria, Lead, Brachial neuritis, Diabetic amyotrophy
Autonomic	Botulism, porphyria, GBS, vincristine Amyloid, chagas d/s, paraneoplastic

● Poliomyelitis

Onset 7–14 days. Acute, ascending, asymmetrical, flaccid paralysis (proximal > distal). It takes 24–48 hr. to onset of full paralysis. There is areflexia (DTR lost) but pupils are normal.

● Botulism

Onset of paralysis b/w 1½–2½ days. There is acute descending symmetric flaccid paralysis (proximal > distal). Reflexes are normal or ↓. Pupils are dilated (mydriasis), diplopia, loss of accommodation

● Diphtheria

Onset of paralysis is b/w 1–8 week. There is acute descending symmetrical quadriplegia, areflexia, ophthalmoplegia, blurred vision, palatal paralysis.

● Lead intoxication

Peripheral neuropathy is mainly motor type (motor delays on nerve conduction). Wrist drop / foot drop (lead palsy)

● Arsenic intoxication

Chronic arsenic poisoning results in peripheral neuropathy. Sensory and motor polyneuritis, distal weakness is seen.

Drug induced myopathies

- Lipid lowering agents --- Statins, fibrates, nicotinic acids
- Glucocorticoids
- Zidovudine --- Mitochondrial myopathy with Ragged red fibres
- Alcohol, heroin, cocaine
- D- Penicillamine
- Chloroquine, hydroxychloroquine
- Colchicine.

Some important channelopathies

Disorder	Ion channel involved
● Episodic ataxia -1	K ⁺ channel
● Episodic ataxia -2, Central core ds, SCA-6, Malignant hyperthermia	Ca ⁺⁺ channel
● Familial Hemiplegic migraine, LEMS	Ca ⁺⁺ (PQ type)
● Hypokalemic periodic paralysis	Slow Ca ⁺⁺ channel
● Hyperkalemic periodic paralysis	Na ⁺
● Myotonia congenita, Cystic fibrosis	Cl ⁻

- Anderson-Tawil syndrome or Long QT syndrome 7, is a rare genetic disorder, and is inherited in an AD pattern. A/w episodic weakness (K^+ channel) + arrhythmias (prolonged QT) + dysmorphic features.
- Jervell and Lange-Nielsen syndrome is d/to mutations in the K^+ channels KCNE1 and KCNQ1 genes. A/w episodic weakness (syncope) + deafness + arrhythmias (prolonged QT).

Flaccid Paralysis & neuropathies : Cause

Level/Site affected	D/s or conditions	C/F
Muscle	Inflammatory myopathies	Symmetrical weakness of proximal m/s, extraocular m/s spared
	Polymyositis	M/s dystrophy, skin spared
	Dermatomyositis	Heliotope skin rash +
	Rhabdomyolysis	
	Periodic paralysis Dysselectrolemia	
N-M junction	MG	Symmetrical, proximal, ptosis is hallmark
	ELS	Proximal weakness, Ocular sparing
	Botulism	Acute descending paralysis (proximal > distal)
	Tick paralysis	
	Organophosphates	Blocks Ach-R
Nerves (acute neuropathies)	Diphtheria	Acute symmetrical, descending paralysis, areflexia, ophthalmoplegia (blurred Vn), palatal palsy
	Porphyria	Assymetric motor weakness, a/w severe abdominal pain, proximal m/s weakness
	Lead	Peripheral motor neuropathy, wrist/ foot drop
	Vasculitis SLE, PAN	Mononeuritis multiplex
	Paraproteinemias	
Nerve roots (radiculopathies)	GBS	Acute AIDP, (sensory neuropathy at the onset but later B/L symmetrical, ascending paralysis set in)
	Sarcoidosis	
	Lyme d/s	
	HIV	Sensory neuropathy
	Viral	

AHC

	Polio ASA syndrome	Acute asymmetrical motor paralysis (proximal > distal weakness)
Spinal cord (CST fibres)	Transverse myelitis SACD Infarction Myelopathies (spondylosis)	
Brain	Pontine lesions Multifocal lesions/ infarcts	

LEMS Vs. Myasthenia Gravis

	Lambert-Eaton Myasthenic Syndrome (LEMS)	Myasthenia Gravis (MG)
Disorder of	N_M junction (Presynaptic)	\downarrow in no. of Ach R at post synaptic muscle membrane
Autoantigen	Synaptotagmin	
Auto antibodies against	P/Q type of calcium channel	ACh receptors
M/c involved m/s.	Proximal m/s of lower limbs (pelvic m/s)	Ocular (early ptosis)
Ptosis & diplopia	Not seen (Ocular sparing)	May be +nt in 70%
Response on repetitive stimulation	Incremental	Decremental (Ms fatigue on repeated stimulation)
Response to exercise	\uparrow Ms strength	
DTR	\downarrow or absent	Preserved, ANS normal
Most commonly a/w	Oat cell type of (SCLC) & responds to guanidine	Thymic hyperplasia (66%), thymoma (10%)
Response to tensilon (edrophonium)	No	Improves (Provocative test used for d/g)
Female preponderance	No	+

- Most sensitive test for MG - SFEMG (Single fibre EMG).
- Most commonly used electrodiagnostic test for MG - Repetitive nerve stimulation test.

D/S OF JOINTS (ARTHRITIS)

RA

- Symmetrical inflammation of peripheral joints with progressive destruction of peri-articular structure.
- Chronic arthritis but acute onset is also seen in ~10% cases.
- First change ---synovium becomes edematous i.e. ↑ fluid content → thickening → Then hypertrophy and pannus formation which is the hallmark of d/s.
- Pannus contains inflammatory cells lymphocytes + plasma cells+ fibroblasts+ small blood vessels)
- Swelling of PIP
- A/w HLA-DR₁ (In India) DR₄ (In other countries)
- M/c site in spine : Upper cervical spine (Atlanto axial dislocation and cervical cord compression), although axial skeleton is usually spared
- M/c symptom is pain aggravated during movements.
- Becker's cyst⁺
- Most specific autoantibody used to evaluate cases of RA --- Anti-CCP
- RF are antibodies usually of IgM class which are directed against F_C fragment of IgG
- M/c tendon ruptured in RA : extensor digitorum communis > EPL > EDP.
- Characteristic changes
 - (a) Z deviation of hand d/to radial deviation of hand at wrist & ulnar deviation of finger & palmar subluxation of proximal phalanges (Z deviation)
 - (b) Swan neck deformity
 - (c) Hitch hiker's thumb d/to extension at 1st IP +, flexion of 1st MCP + loss of thumb mobility and pinch.
 - (d) Hammer toes
- X-ray features:
 - (a) Juxta-articular osteopenia
 - (b) Bone erosions
 - (c) Narrowing of joint space d/to loss of articular cartilage.
 - (d) Characteristic is **sparing of DIP (&hip) joints.**
- T/t: **Methotrexate** remains DMARD of choice. Naproxen is best analgesic to use. Biologics are recent drugs —
TNF inhibitors: Etanercept, infliximab, adalimumab
Anakinra: IL-1 receptor antagonist
Rituximab: Chimeric antibody against CD20
Abatacept: Fusion protein CTLA4 + Fc portion of IgG.

Arthritis According to no. of joints involved

Mono-articular	Pauci/oligo (2-4)	Polyarticular (≥ 5 joint)
● Gout	● Reiter's disease	● RA (Rheumatoid)
● Gonococcal	● Psoriatic A~	● SLE
● TB	● IBD	
● Neuropathic		
● Septic		
● Lyme disease		
● Leg-Perthes disease		
● Hemophilia		

RF in Arthritis

	Features	Examples
● Seropositive arthritis	RF +ve in (True +ve)	RA,
	Falsely + ve RF	TB, Leprosy, malaria, infectious mononucleosis, etc.
● Seronegative arthritis	RF -ve, Strong F/H	AS, Behcet's, Psoriasis, Reiter's, Reactive arthritis, still's d/s, whipple's
● ANA is a/w		Polymyositis, SLE, RA, Sjogren's, fibrosing alveolitis

Joints involved in Arthritis

Arthritis	Type	M/c joints	Less common	NOT involved	Nature
RA	Poly	MCP, PIP, MTP	Knee, Cervical spine	DIP, hip	Erosive, painful
SLE	Poly	MCP/wrist		OA	Non-erosive
OA	Poly	DIP > CMC in hands, Knee, Sacro-iliac		Wrist/MCP	May be erosive
Psoriatic	Pauci/oligo	PIP, DIP			Painful
AS	Mono	Axial skeleton (Spine)	Hip	?hand	Inflammatory
Gout	Mono	MTP of great toe			Erosive, painful

→ Mnemonic to remember

MRS. DOP MCP involved in RA and SLE
 DIP involved in OA and Psoriasis

- Arthritis in SLE is always non-erosive.
- Joints of the hands are usually NOT involved in AS.
- In RA & other inflammatory arthritis bony erosions are seen.
- Anti TNF- α (Infliximab) is NOT used in SLE
- Uses of Anti TNF- α (Infliximab) --- RA & CD
- Uses of Adalimumab --- RA
- Uses of Etanercept --- RA, JRA, & Psoriasis.
- Felty syndrome is --- Chronic RA + splenomegaly + neutropenia (<1500 cells)
- Caplan syndrome is --- Pulmonary nodule in a patient of pneumoconiosis.
- In RA m/c involved joints are --- MCP of index finger > wrists > PIP > MTP > Knee, ankle, shoulder, elbow.
- In OA m/c involved joint is DIP f/b CMC joint of thumb. MCP and wrists are spared.
- M/c cause of septic arthritis in infants is H. influenzae.
- M/c cause of septic arthritis in older children/adults --- staph. aureus.

Arthritis according to evolution

- Chronic : OA
- Intermittent : Gout
- Migratory : Rheumatic fever, gonococcal, viral, meningococcal, Lyme's d/s.
- Additive : RA, Reiter's syndrome

OSTEOARTHRITIS (OA)

- **Heberden's nodes** (bony enlargement of the DIP joint) are the m/c form of idiopathic osteoarthritis.
- A similar process at the PIP joint leads to **Bouchard's nodes**.
- **Gelatinous dorsal cysts** may develop at the insertion of the digital extensor tendon at base of distal phalanx.

→ Degenerative joint d/s
 → Decreased (narrow) joint space
 → DIP joint are involved more than PIP

} 3 'D'

- Knee joint is commonly affected in Asians (genu varum) while hip in Westerns.
- 1st MCP — radial subluxation of 1st metacarpal base
- Spine : sclerosis + narrowing of IVD .Osteophytosis.
- Earliest pathological change --- \uparrow water content & \downarrow proteoglycans in cartilage matrix
- Repeated weight bearing leads to fibrillation

- Earliest symptom — pain (Dull pain manifests on starting of activities from rest)
- Erosive OA: Inflammatory form of OA predisposed in postmenopausal females.

Radiological changes in OA

- Narrowing of joint space, subchondral sclerosis & cysts, osteophytes formation, loose bodies & deformity of joint (Genu Varum).

ANKYLOSING SPONDYLITIS

- Ankylosing spondylitis is an inflammatory disorder of unknown etiology that primarily affects the axial skeleton. (Hand joints are NOT involved).
- Usually begins in 2nd or 3rd decade.
- A/w **HLA-B 27** allele
- Diagnostic criteria are :

1. Definitive radiological sacroilitis

+

2. Any of these 3

- H/o back pain (inflammatory)
- Limitation of movement of lumbosacral spine
- Limited chest expansion

- **Sacroilitis** is the *earliest* manifestation with features of enthesitis and synovitis.
- **Enthesitis**, the site of ligamentous attachment to bone is primary site of pathology. Enthesitis is a/w prominent edema of adjacent bone marrow and often characterized by erosive lesions that eventually undergo ossification.
- **New bone formation (syndesmophytes)** c/b found within inflammatory infiltrate, which is seen in ligamentous and periosteal zones (not at muscle attachment site)
- Bone mineral density is diminished in spine and proximal femur in early course of disorder.
- Radiological features:
Bamboo spine (Loss of lumbar lordosis in lumbar spine)/
Rugger jersy spine, enthesitis, syndesmophytes, diffuse osteoporosis, **squaring of vertebrae** occurs
- Common sites costosternal junction, spinous processes, iliac crests, greater trochanters, ischial tuberosities, tibial tubercles and heels.
- M/c extra articular manifestation is acute anterior uveitis.
- M/c serious complication of spinal d/s is spinal # involving cervical spine. These #'s are commonly displaced.
- T/t : NSAIDs, Anti-TNF α (infliximab, etnacept, adlamumab), sulfasalazine, thalidomide

GOUT VS. PSEUDOGOUT

Gout	Pseudogout/chondrocalcinosis
<ul style="list-style-type: none"> ○ Erosive painful arthritis in 1st MTP jt / great toe (m/c site) ○ Deposition of <u>monosodium biurate</u> crystals/ tophi (needle shaped, <u>negatively</u> birefringent) ○ 1st MTP joint affected ○ ↓ Renal excretion of urates in m/c cause of gouty arthritis ○ M > F affected. Large joints c/b affected. 	<ul style="list-style-type: none"> ○ Mc site — Knee [Meniscj calcification] ○ Deposition of CPPD (weakly positive birefringent rhomboid) crystals ○ Chondrocalcinosis (calcification of articular cartilage) is diagnostic ○ AD form is a/w mutation in ANKH gene ○ Secondary form is a/w hypothyroidism, hemochromatosis, hypomagnesemia, diabetes, ochronosis

- *Podagra* is a painful condition of the big toe caused by gout.
- *Ochronosis* is deposition of homogentisic acid in joints in alkaptonuria.
- *Tophi* is deposition of negatively birefringent monosodium biurate crystals in joints.

○ *Drugs for acute gout are :*

- NSAIDs (esp. indomethacin) is the first line drug
- Colchicine
- Corticosteroids, ACTH

○ *Drugs for chronic gout are :*

- Allopurinol : Xanthine oxidase inhibitor prescribed for chronic gout or gouty arthritis and works by ↓ing uric acid in the body. It is used to prevent gout attacks, not to treat them once they occur.
- Probenecid
- Sulfinpyrazone : Uricosuric drug which prevents attacks.
- Uloric (febuxostat)
- Krystexxa (pegloticase)

CHARCOT'S JOINT (Neuropathic jt disease)

- Progressive destructive arthritis a/w loss of pain / proprioception or both. Normal muscular reflexes that modulate joint movements are also decreased. So joints are subjected to repeated trauma resulting in progressive cartilage and bone damage.
- *Diabetes mellitus is the most frequent cause.*
- Other causes are tabes dorsalis, congenital insensitivity to pain, meningomyelocele, peroneal muscular atrophy, Syringomyelia, amyloidosis, leprosy.

Antiphospholipid Syndrome (APLA/ Lupus anticoagulant)

- Syndrome a/w antiphospholipid and anticardiolipin antibody in circulation (*circulating anticoagulants*).
- Coagulation profile is prolonged. Following coagulation abnormalities are found:
 - Arterial and venous thrombosis (Unexplained Juvenile DVT)
 - Thrombocytopenia
 - Thromboembolization (stroke, CNS complications)
 - Hepatic vein thrombosis (Budd Chiari syndrome)
- Obstetric C/c : **Repeated spontaneous abortions**
- D/g : ↑aPTT & ↑ Russell viper venom time (dRVVT) is more sensitive.
- Most specific antibody is anti-β₂glycoprotein (GPI) antibody
- T/t : Bleeding responds to steroid but clotting does not.
- *Sneddon's syndrome* is triad of livido reticularis + stroke like episodes + HTN a/w APLA.

Circulating anticoagulants

Anti Phospholipid antibodies in circulation are of two types:

Lupus anticoagulant (LA)	Anticardiolipin antibody
<ul style="list-style-type: none"> ○ C~ against platelet PF3 ○ This prolongs aPTT (90%) & sometimes PT ○ Addition of normal serum does not correct prolonged aPTT (addition of phospholipid to the plasma is required for correction of aPTT) 	<ul style="list-style-type: none"> ○ C~ against cardiolipin ○ This produces false +ve syphilis serology

ENDOCRINO

→ PTH & Vit. D₃ receptors :- are present on osteoblasts

PTH → activates osteoblasts → release IL-1 → Stimulates osteoclast to remove Ca⁺⁺ from bone → hypercalcemia

→ Calcitonin receptors are present on osteoclasts (calcitonin inhibit osteoclastic activity) → hypocalcemia

Hyperparathyroidism (↑ PTH)

Feature	Primary	Secondary	Tertiary
Serum Ca ⁺⁺	↑	N, ↓	↑
Serum P	↓	+ N, ↑	P (↑ALP)
ALP	↑	↑	↑
Causes	M/c cause (90%) is <u>Single adenoma</u> , Multiple adenoma (4%) Nodular hyperplasia (5%) Carcinoma (1%)	Secondary to renal failure, osteomalacia, rickets, malabsorption	In some cases of 2° H~ continuous stimulation of parathyroid results in 3° H~ α1-Hydroxylase deficiency ↓ Autonomous hyperactive chief cells
Remark	M/c parathyroid disorder	Hypocalcemia leads to secondary stimulation of gland ↓ Parathyroid gland hyperplasia, Hyperphosphatemia (d/to renal retention & ↑ bone breakdown)	

Osteitis Fibrosa Cystica

- Seen in 2° hyperparathyroidism.
- Marked osteoclastic activity can be seen & resorbed bone is replaced by fibrous tissue to produce the so called "Brown tumours" as a consequence of patchy osteolytic lesions throughout the skeleton & pathological # may occur
- Resorption affects terminal phalanges in hands & alveolar margins in jaw. Calcilytics are drugs that antagonize the calcium-sensing receptor and promote PTH secretion.

HYPOPARATHYROIDISM (HP)

- M/c seen following thyroidectomy.
- Characterised by Bones, groans, psychic moans & abdominal stones.
- Lab/f - ↓ Serum & urine Ca⁺⁺, ↑ S.PO₄⁻⁻⁻, ALP = N
- Cl/f : The signs and symptoms of hypoparathyroidism include evidence of latent or overt **neuromuscular hyperexcitability** due to hypocalcemia. The effect may be aggravated by hyperkalemia or hypomagnesaemia.
 - Tetany, seizures, hyperactive DTRs
 - Trousseau's sign/ phenomena* (carpo-pedal spasm after application of cuff)
 - Tingling of lips / hands, abdominal cramps
 - Chvostek sign*: facial m/s contraction on tapping facial nerve in front of ear.
 - Paresthesias
 - Laryngospasm, Bronchospasm
 - Prolonged Q-T interval on ECG
- Basal ganglia calcification & cataract may occur.

PseudoHypoParathyroidism (PHP)

Type	G5α deficiency	Urine cAMP	Ca ⁺⁺	PO ₄	PTH	1,25 (OH) ₂ D	Pheno type
HP		N		↑	↓	↓	
PHP Ia	100%	↓	↓	↑	↑	↓	AHO
PHP Ib	0%	↓	↓	↑	↑	↓	N
PHP Ic		↓		↑	↑	↓	
PHP II	0%	N	↓	↑	↑	↓	
PPHP (Pseudo-pseudo)	Partial	N	N	N	N	↓	AHO

- Pseudohypoparathyroidism (PHP)* is d/to end organ/ receptor defect making them refractory to the action of PTH. 4th & 5th metacarpals may be short.
- PTH level is low in HP(hypo), high in PHP, normal in PPHP.
- Albright's hereditary osteodystrophy (AHO)*: is found in PHP Ia & PPHP). Typically, patients have short stature, round facies, brachydactyly, obesity, and ectopic soft tissue or dermal ossification(s) (osteoma cutis). In the calvaria, this may manifest as hyperostosis frontalis interna. Intracranial calcification(s), cataracts and band keratopathy, subcutaneous calcifications, and dental hypoplasia.

THYROID DISORDERS

- Serum RT_3 is useful for d/g of nonthyroidal illness syndrome
- I^{131} uptake (RAIU) is \uparrow in 'hot' nodule (d/to uptake by functional tissue) & 0 (no uptake) in 'cold' nodules
- Serum TSH is single best overall test for thyroid profile.
- Cord blood FT_4 and TSH are used to screen hypothyroidism in newborn.
- TSI (Thyroid stimulating immunoglobulins) are immune marker for Graves' disease
- Anti-thyroid antibodies are useful for d/g of auto-immune thyroiditis (anti-microsomal Ab is the best test). Anti-microsomal Peroxidase antibodies (TPO) have highest titre in Hashimoto's thyroiditis & moderately elevated in Graves' disease.

THYROIDITIS

Type	De Quervain's	Riedel's	Hashimoto's
Also	Granulomatous k/as	Painless	Lymphadenoid goitre
Cause	Precipitated by viral infection/ URI	Compression	Familial, Anti-TPO/TBG/ microsomal antibodies +
Thyroid Gland	Firm, tender, enlarged	Stony hard, painless goitre	Sporadic goitre in children
TFT	Hyperthyroidism	$\downarrow Ca^{++}$, Hypo-thyroidism	Hyper \rightarrow hypo \rightarrow N
Lab	\uparrow ESR, \downarrow RAIU	Mediastinal/ RP fibrosis	Follicular & Hurthle cell hyperplasia, Plasma cell/lympho infiltration
Rx	NSAIDs	Tamoxifen/ steroids, Partial removal of gland.	Thyroxine

TRH Stimulation Test

- TRH stimulates the release of TSH, Prolactin, GH
- TRH induced GH stimulation may occur in acromegaly, anorexia nervosa, uremia, PEM (conditions with \uparrow Basal GH level)
- TRH stimulation is useful in supporting a d/g of hyperthyroidism, recurrent acromegaly, Gn secreting tumours

- \rightarrow T_4 & TSH levels are unaffected by gout.
- \rightarrow $T_3 \downarrow \downarrow$ occur during starvation

HYPERTHYROIDISM

- **Pretibial myxoedema** may be seen.
- *Jod- Basedow phenomena* is excessive thyroid hormone synthesis d/to \uparrow iodine exposure.
- *Wolff-Chaikoff effect* is suppressive action of excessive iodides, which transiently inhibits thyroid I^- organification.
- *Pemberton's sign* is compression effect of large retrosternal goitre.
- *Pendred syndrome* is sensori-neural deafness + partial organification of thyroid.
- *CVS manifestations:*
 - \uparrow in cardiac output
 - Palpitations, systolic hypertension
 - Sinus tachycardia (m/c manifestations)
 - Hyperdynamic precordium
 - Mid systolic murmurs (systolic ejection click)
 - Means -Lerman scratch : systolic scratchy sound
- **T/t :**
 - PTU, carbimazole, methimazole (active metabolite of carbimazole) --- All inhibit TPO
 - Propranolol
 - Radio iodine (I^{131}) is useful

- \rightarrow *DOC in thyrotoxic crisis is large doses of propylthiouracil as it blocks T_4 to T_3 conversion*

Hypothyroidism

Congenital:

- **Normal birth weight & length**, prolongation of physiological jaundice, feeding difficulties, constipation, coarse facies, low hair line
- O/E there is stunting of growth, **delayed bone age**, wide open fontanels, hypotonia.
- **Epiphyseal dysgenesis** is pathognomonic
- *Disproportionate dwarfism* (infantile proportions are retained). *Precocious puberty* may occur
- Neonatal screening tests are --- TSH, T_4 , T_3 estimation \uparrow **TSH (most specific)**, \downarrow T_4 , T_3 may be normal
- Epiphyseal centres that are normally present at birth are upper end of tibia, lower end femur in the knee joint &

talus, calcaneum, cuboid in ankle joint. These centres may be absent in X ray in congenital hypothyroidism.

Acquired (Myxoedema):

- D/t destruction of thyroid d/to autoimmune lymphocytic infiltration, irradiation, following surgery
- **Presents with stunting of growth**, cold intolerance, excess sleepiness, delayed bone age, subnormal intelligence
- Hypothyroidism in a pt with IHD is treated by --- low dose of levothyroxine .
- Hung up reflex: A DTR in which after a stimulus is given & reflex action takes place. The limb slowly return to its neutral position. Relaxation phase is prolonged.

Polyglandular Autoimmune Syndromes (PGA)

○ PGA I:

- Autosomal recessive, mutations in APECED gene
- Mucocutaneous candidiasis, hypothyroidism, hypoparathyroidism, adrenal insufficiency, dental enamel hypoplasia, malabsorption, vitiligo, pernicious anemia, hypogonadism, alopecia etc.

○ PGA II:

- Polygenic inheritance, a/w HLA- DR3 and DR4, adult onset, more in female
- A/w hypothyroidism, Grave's d/s, MG, celiac d/s, **type1 DM**, adrenal insufficiency, hypophysitis, vitiligo, pernicious anemia, hypogonadism, alopecia etc

→ Autoimmune hypothyroidism is a/w --- PGA

→ In t/t of hypothyroidism the efficacy of drug t/t is assessed by testing TSH

→ Drugs that have profound effect on the thyroid function --- Amiodarone, PAS, Li

→ Hypothyroidism is a/w ↑ed level of --- Cholesterol.

→ Weight gain is seen in → hypothyroidism, insulinoma, craniopharyngioma.

Some conditions a/w hypo-/hyperglycemia

Hypoglycemia	Hyperglycemia
○ Hypopituitarism	○ Hyperpituitarism (Acromegaly)
○ Adrenal insufficiency	○ Hyperadrenalism, Cushing syndrome
○ Hepatitis	
○ Hypothyroidism	
○ Insulinoma	

→ Mineralocorticoids are synthesized by glomerulosa, glucocorticoids by fasciculata and sex steroids by reticulata (Remember GFR for Mineralo-, gluco-, sex steroids respectively.)

→ Liddle's syndrome : AD disorder that mimics hyperaldosteronism. Defect in sodium channels which leads to continuous activation of Na^+ -channels leading to increased Na^+ absorption in renal tubules — both renin & aldosterone are low

→ Bartter's syndrome : secondary hyperaldosteronism (d/t to high renin) but normal BP, no edema.

Hyperaldosteronism Vs Addison's Disease

	Conn's Syndrome (1° Hyper-aldosteronism)	Cushing's Synd (Glucocorticoid excess)	Addison's Ds. (Adrenocortical insufficiency)
Cause	- Adenoma is the m/c cause - B/L cortical hyperplasia is the m/c cause of 1° hyperaldosteronism. - Adrenal carcinoma	Iatrogenic steroids m/c cause, Pituitary adenoma ↑ secretion of ACTH from pituitary (Cushing's ds) / Ectopic production (Oat cell Ca)	Autoimmune / idiopathic (m/c) TB, Amyloidosis, Hemosiderosis . Drugs: Phenytoin, Rmp, Opiates, aminoglutethimide, KTZ, metyroponc, mitotane (medical adrenalectomy) Exogenous steroids
C/f	Features of salt / water retent ⁿ Hypermnatremia, Hyperchlorhydria, Hypervolemia, Hypokalemic alkalosis (episodic weakness / Tetany) <u>Hypertension</u> (↑ DBP) Polyuria, Polydipsia Ankle / pedal edema not seen d/to escape phenomena Alkaline urine [Remember all ↑ except K^+]	Features of water retent ⁿ Moon facies with plethora, Buffalo hump, Muscle wasting/ weakness, Abdominal striae, Renal calculi, HTN <u>Osteoporosis</u> Hirsutism, amenorrhea, <u>Hyperglycemia</u> , Glycosuria, (Anti insulin effect of ↑ cortisol)	Bronze pigmentation of skin & mucosa (Hyperpigmentation) ↓ ECF volume Hyponatremia & Hyperkalemia (metabolic acidosis) <u>Hypoglycemia</u> (↓ Gluconeogenesis) Calcification of adrenals Weakness/ asthenia (m/c symp) Weight loss ↓ Na^+ Cl^- & HCO_3^-
D/g		Abnormal dexamethasone suppression test	<u>ACTH stimulation test</u>
Rx			IV fludrocortisone for acute adrenal insufficiency

OBESITY

- Is a state of excess adipose tissue.
- Pathological features and complications a/w obesity:
 - Glucose intolerance
 - Insulin resistance.
 - HTN, ↑ed risk of CVS d/s, gout, OA.
 - Hypothyroidism
 - ↓ GH
 - Cortisol production and urinary metabolites (17-OH steroids) ↑ed.
 - Menstrual irregularities in females esp. oligomenorrhea and PCOS
 - **Obstructive sleep apnea** and obesity hypoventilation syndrome.
 - *Gallstones*
 - **Cancers of colon, rectum and prostate in male and cancers of gall bladder, endometrium, cervix, ovaries and breast in female.**
 - ↑ed risk of osteoarthritis and gout.
- Conditions a/w obesity — Cushing, Hypothyroidism, Insulinoma
- Syndromes a/w obesity
 - Prader-Willi
 - Laurence Moon Biedl (LMB)
 - Cohen
 - Carpenter
 - Ahismom
- W:H ratio
 - >1 in men : Obesity
 - > 0.85 in women : Obesity
- T/t:
 - Reduced caloric intake is the cornerstone of obesity t/t
 - Exercise, lifestyle modifications
 - Drugs
 - Phentermine:** amphetamine like drug which acts centrally by reducing appetite
 - Fenfluramine :** SRI
 - Fen-Phen :** Combination of above two (Phentermine + Fenfluramine)
 - Sibutramine:** NSRI
 - Metformin :** In patient with obesity and type 2 DM

- *Surgery (Bariatric surgery) is required for morbid obesity (BMI > 40) or BMI > 35 with comorbidity*
- *Dual energy X-ray absorptiometry (DEXA) provides the best assessment of total body fat.*

MULTIPLE ENDOCRINE NEOPLASIA (MEN SYNDROME)

Tumour Type	MEN 1 (Wermer's)	MEN 2a (Sipple's)	MEN 2b
Parathyroid	>80%	50%	Rare
Pancreatic	75%	-	-
Pituitary	60%	-	-
Medullary thyroid ca.	-	>50%	80%
Pheochromocytoma	-	20%	60%
Mucosal & GI ganglioneuromas	-	Rare	>90%
Lipoma	Occasional		
Adrenocortical adenoma	Occasional		
Carcinoid	Occasional		
Thyroid adenoma	Occasional		

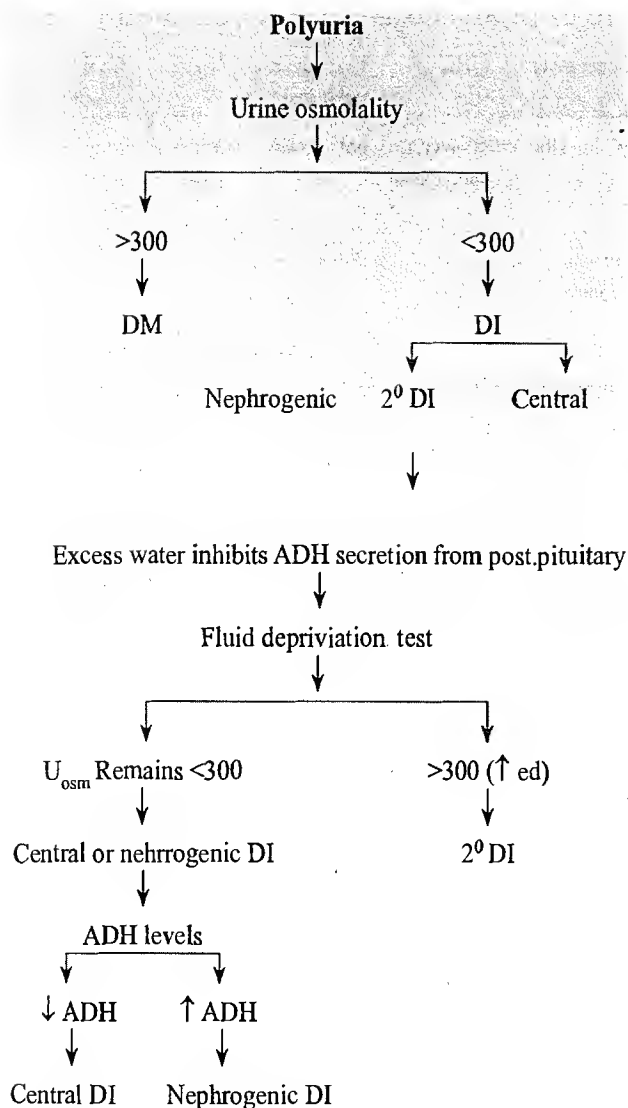
- *When medullary thyroid carcinoma & pheochromocytoma are a/w hyperparathyroidism then it is called MEN 2a or Sipple syndrome & if they are a/w mucosal neuromas and marfanoid habitus it is MEN 2b*
- *Pheochromocytoma should be operated first then medullary carcinoma of thyroid in MEN - II*
- *In MEN - I hyperparathyroidism is treated 1st & when Ca⁺⁺ levels are controlled, treat ZES or pancreatic islet tumours.*
- *Tumour most commonly a/w MEN 1 is parathyroid adenoma*

Remember that :

- Oliguria is urine output <400 ml/d or <20 ml/H
- Anuria is urine output 0-50 ml/d
- Polyuria is urine output > 3L/d.

APPROACH TO POLYURIA

- Two mechanism are involved :
 1. More excretion of water
(due to osmotically active substances)
 2. Failure of reabsorption of water
- Approach algorithm:



Diabetes Insipidus (DI)

- DI is caused by deficiency of vasopressin (ADH/AVP) leading to impaired absorption of water producing **polyuria, polydipsia**
- Types: Nephrogenic, Central (pituitary) & 2°. Secondary (2°) DI is the m/c type.
- Sarcoidosis can cause any type of DI.
- Cardinal features --
 - Plasma**: hypernatremia, ↑ osmolality (>290)
 - Urine** --- ↓ sodium U. $\text{Na}^+ < 20$, ↓ osmolality ($\text{U}_{\text{osm}} < 300 \text{ mosm/l}$) d/to dehydration
- D/g -- Water deprivation test is useful.
- D/d -- Hypothyroidism, hyperadrenalism, and DM should be ruled out.

T/t : Desmopressin is drug of choice

Nephrogenic---Chlorthiazide (for Li induced DI)

Central --Desmopressin (dDAVP nasal spray) is recognized as the drug of choice for central DI.

Vaptans are aquaretic drugs, which act by antagonist action at aquaporin -2 (V2)-receptors. They are indicated in hypervolemic and euvoletic patients. Only 2 vaptans are FDA approved:

- **Tolvaptan** (Oral drug given in dose of 15 mg OD)
- **Conivaptan** (I/v drug)

Type	Causes	T/t
Central	Congenital	
	Acquired <ul style="list-style-type: none"> - Surgery - Trauma - Radiation - Sarcoidosis 	Desmopressin
Nephrogenic	Lithium, cisplatin, Amphotericin B, aminoglycosides, Dyselectrolyemia ($\downarrow \text{K}^+$, $\uparrow \text{Ca}^{++}$), ATN, Sarcoidosis	
2° DI	Psychogenic : OCD	
	Dipsogenic (Threshold for thirst is ↓ed), Drugs : Carbamazepine, Li Sarcoidosis	
	Iatrogenic	

→ Sarcoidosis can cause all types of DI.

→ Lithium can induce hypothyroidism, DI, and parathyroid adenoma causing 1° hyperparathyroidism.

→ 2° DI is the m/c cause of DI.

Psychogenic Polydipsia

- Both plasma & urinary osmolality are ↓ed
- Water deprivation test is useful in d/g. Initial low urine osmolality gradually increases with the duration of water deprivation in this condition but not so in DI
- Seen in schizophrenic or OCD pt.

SIADH

- Syndrome of inappropriate ADH secretion (SIADH) is caused by excess vasopressin release leading to increased absorption of water producing hyperosmolar or concentrated urine (plasma is diluted i.e. **hypervolemia** & urine is concentrated). Findings are opposite to DI
- *Imp. causes*
 - Head trauma
 - Infections (meningitis, encephalitis, AIDS)
 - *Malignancy* (Oat cell ca/SCLC, thymoma)
 - *Drugs* (Vincristine, Chlorpropamide, Carbamazepine, oxytocin)
 - Other --- porphyria, hypothyroidism
- Cardinal features:
 - Plasma* --- **hyponatremia**,
↓ **osmolality** (< 280), ↓ **BUN** (< 10),
↓ **hypouricemia** (< 4)
 - Urine* : ↑ **sodium U. Na⁺** > 20, ↑ **osmolality** (Uosm)
- Concentration of other electrolytes is also low in plasma e.g. hypomagnesemia
- SIADH is a diagnosis of exclusion. Absence of cardiac, liver, or renal disease. *No edema*. Normal thyroid and adrenal function
- **T/t** --- Restrict fluid intake, give hypertonic saline. Lithium and demeclocycline are only drugs for SIADH. fludrocortisone is also useful. Demeclocycline antagonises ADH and can lead to DI.

Cerebral salt wasting [CSW]

- Suspected when there is hyponatremia in a hypotensive patient with associated CNS d/s.
- Urine volume is initially high but later it becomes normal or low once patient starts dehydrating.
- *Lab/f*: Hypovolemia (clinical evidence of volume depletion), ↑↑ **sodium U Na⁺** ↑↑ **urine flow rates**, net sodium loss is very high (+++).
- ↑ **Secretion of BNP**.

→ SIADH and HRS (hepatorenal syndrome) are 2 conditions which are diagnosis of exclusion.

→ Hypothyroidism is a/w increased level of --- Cholesterol

D/d of DI, Psychogenic polydipsia, SIADH, CSW

Parameter	DI	Psychogenic polydipsia	SIADH	CSW
Clinically	Polyuria, polydipsia	polydipsia	Well hydrated pt	Dehydrated, hypotensive pt
Plasma volume	↓	Slight ↑	↑	↓
Plasma Na ⁺	↑	↓	↓	↓
Plasma osmolality	↑	↓	↓	↓
Urine osmolality	↓	↓	↑	↑↑
Urine volume	↑	↑	↓	↑ initially ↓ later
Plasma ADH	↓	↓↓	↑	↓
Plasma aldosterone	Normal	Normal	↑	↓

Pheochromocytoma

- Arises from paraganglionic cells of ANS
- M/c site of origin --- adrenal medulla
- M/c extraadrenal site is --- paravertebral sympathetic ganglions in organ of Zuckerkandl (near aortic bifurcation)
- IOC is CT Scan (for adrenal p~)
- IOC for locally recurrent, metastatic, ectopic and extraadrenal p~ is MIBG scan (MIBG > MRI > CT)
- **Rule of 10** : 10% are extra-adrenal, 10% of sporadic adrenal p~ are bilateral, 10% are malignant, 10% are not a/w hypertension.
- Locoregional spread is seen.
- Hormone secreted in pheochromocytoma: NE (max^m), E, DA, VME (in urine).

ORAL DISEASES

- **Strawberry gingiva/gums** are seen in --- Wegner's granulomatosis (Red purplish granular gingivitis)
- Strawberry tongue is seen in --- Kawasaki scarlet fever
- Gingival/gum hypertrophy or swelling is seen in --- AML (M5)
- Gingival/gum hyperplasia is seen with the use of --- Phenytoin, CCBs (nifedipine), cyclosporine, etc.

RESPIRATORY SYSTEM

Sputum

- Pink frothy sputum is seen in --- Pulmonary edema
- Sputum containing Charcot -Leyden crystals, and crushman's spirals seen in --- Bronchial asthma
- Current jelly sputum is seen in --- Klebsiella pneumonia.

Bronchial breathing :

Bronchial breathing anywhere other than over the trachea, right clavicle or right interscapular space is abnormal.

Presence of BB would suggest:

- Consolidation
- Cavitation
- Complete alveolar atelectasis with patent airways
- Mass interposed b/w chest wall and large airways
- Tension Pneumothorax
- Massive pleural effusion with complete atelectasis of lung.

Dyspnea

- *Orthopnea* (dyspnea on recumbency) and *nocturnal dyspnea* are seen in asthma, GERD, LVF, Obstructive sleep apnea. Orthopnea in heart failure is d/to redistribution of blood from peripheral veins.
- *Platypnea* (dyspnea that worsens in the upright position) is a/w deficient abdominal musculature, A-V malformations at lung bases.
- *Trepopnea* : dyspnea occurs only in lateral decubitus position most often in patient with heart disease.
- *Constant dyspnea* is mostly d/to COPD but also seen in ILD (e.g. pulmonary fibrosis), pulmonary vascular diseases.

Pulmonary Embolism

- A patient of pulmonary embolism presents with dyspnea, tachypnea, hypotension, cyanosis, cough, hemoptysis, pleuritic chest pain, syncope
- **Dyspnea** is most frequent symptom and **tachypnea** is most frequent sign.
- Right heart failure is the usual cause of death from PE.
- **MDCT (Multidetector CT)** is the principal imaging test now a days for the d/g of PE.
- CXR may be normal or near normal. Focal oligemia (Westermarck's sign), wedge shaped density above diaphragm (hampton's hump), and enlarged right descending

pulmonary artery (Pall's sign) may be seen. On transthoracic echo ' McConnell' s sign is seen

- On ECG most cited abnormality is sinus tachycardia and **S1Q3T3 sign**.
- Lung scans (V/Q scan) is now the second line diagnostic test for PE. Pulmonary angio is specific test.
- Individuals with hypercoagulable states (esp. inherited factor V leiden) are predisposed. The quantitative plasma D-dimer ELISA level is elevated in > 90% of patients .
- M/c source of emboli : Proximal vein of LL (femoro-popliteal/iliac).
- T/t : Anti-coagulation

→ M/c source of DVT → Calf veins

ASTHMA

- Affects small airways (terminal bronchioles)
- Curschmann's spirals (mucus plugs + epithelial cells), Charcot Leyden crystals (crystalline material within eosinophils) are seen in sputum.
- **Creola bodies** are seen.
- **ASTHMA TRIAD [SAMPTER'S TRIAD]**
Hypersensitivity to aspirin + Nasal allergy/ polyposis + Bronchial asthma.

Chronic Bronchitis

- **Reid's index** is ↑ed (>0.4).
- Hyperplasia and hypertrophy of mucous glands of bronchus.
- CXR: Prominent bronchovascular markings.

Primary pulmonary hypertension (PPHN)

- Signs : Loud P2, left parasternal heave, ↑JVP.
- NO have a role in t/t.

PNEUMONIA

Pneumococcal

- **lobar pneumonia**
- **Cl/f** : *Flushed* app., tachycardia, tachypnea, males affected more. Sputum is **rusty**
- Type 3 is a/w lung abscess.
- **Austrian triad** of pneumococcus pneumonia + infective endocarditis + meningitis.

Staphylococcal

- Bronchopneumonia / **Lobular** pneumonia
- **CI/f** : Affects elderly
- Shaggy, thin walled cavities seen in CXR k/as **pneumatoceles** are characteristic.
- **C/c** : Empyema in infants

Klebsiella

- Causes community acquired lobar pneumonia (Friedlander's pneumonia)
- **CI/f** : Commonly affects alcoholic, >40 year, diabetic / COPD patients. Current-jelly sputum is seen
- Upper lobe involvement is seen

Pneumocystis carinii

- Also k/as plasma cell or **interstitial pneumonia**.
- Seen in HIV⁺ /immunocompromised or low CMI patient.
- **CI/f** : Fever, dyspnea, dry cough, retrosternal pain worsening on inspiration.
- **B/L** perihilar infiltrates are seen.
- **M/c** X-ray finding is *normal film*.
- **Patho**: Mononuclear infiltration.

Primary/Non-bacteremic

- Acute, life-threatening infection caused by pseudomonas aeruginosa
- Fever, chills, severe dyspnea, cyanosis⁺
- CXR : **B/L** Bronchopneumonia with nodular infiltrates, pleural effusion, *microabscess*⁺

→ *Interstitial pneumonia is most frequently due to influenza virus.*

→ *M/c cause of community acquired pneumonia — Streptococcus pneumoniae (30%) > Mycoplasma (9%)*

→ *M/c cause of overwhelming post-splenectomy infection (OPSI) — Pneumococcus (Streptococcus pneumoniae)*

→ *M/c cause of Hospital acquired (Nosocomial) P~: Enteric gm -ve bacilli [E.coli + pseudomonas + Klebsiella]*

→ *M/c of lobar pneumonia- strepto. pneumoniae (>90%)*

→ *Pneumonia a/w lung abscess --- Klebsiella, pneumococcal, staphylococcal pneumonias*

→ *Pneumonia a/w pneumatocele --- Staphylococcal pneumonia.*

→ *CURB 65 criteria : for predicting mortality in community acquired pneumonia.*

Measles pneumonia

- Multinucleate giant cells called Warthin-Finkeldey cells are seen, which have eosinophilic inclusions (**Giant cell pneumonia**).
- Interstitial mononuclear infiltration is found

Interstitial pneumonia is caused by

- Influenza virus (most frequent cause)
- Pneumocystis carinii
- Mycoplasma
- Legionella

CVS

Named murmurs

Type	Nature	Found in
Uterine souffle	Continuous arterial m~ over uterus	Pregnancy
Mammary souffle	Continuous arterial m~ over breast	Chondrodysplasias
Duroziez	Over femorals	AR
Austin flint's	Mid/late DM	Severe AR
Siegle's		AR
Carry Coomb's	Mid DM	Ac. mitral valvulitis, RF
Gibson's	Continuous/ train in tunnel	PDA
Carvallo's	Early SM	TR, SABE
Graham steel's	Early DM	PR

- **Cruveilhier-Baumgarten murmur** is a venous hum heard in epigastric region (on examination by stethoscope) because of collateral connections between portal & systemic circulation. Seen in portal hypertension.

→ *Usually named murmur are diastolic except Carvallo's and still's murmur (in children), which are systolic*

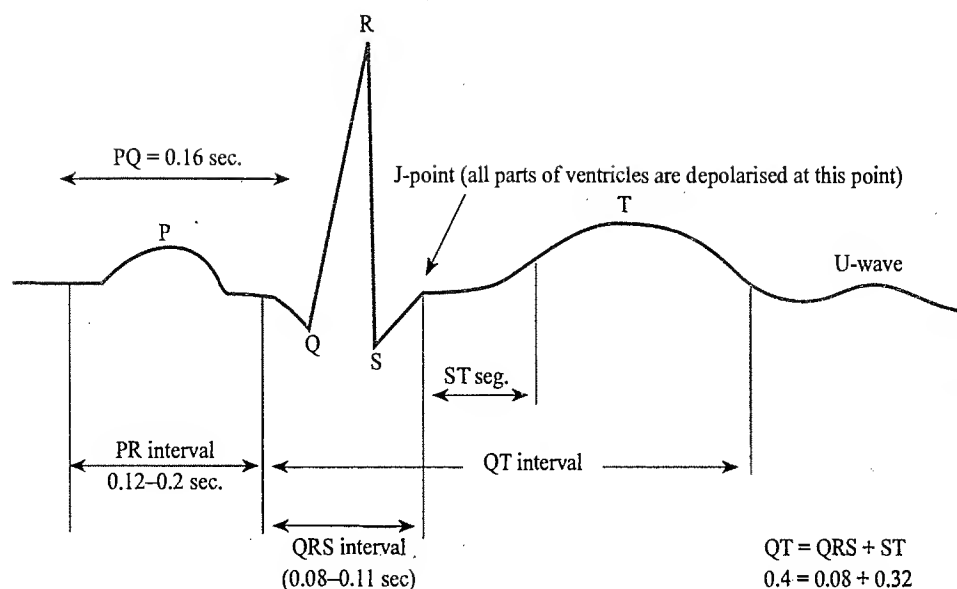
→ *Systolic murmurs are present in AS or PS & MR or TR [Remember SSS Systolic murmur is seen in Stenotic lesion of Semilunar valve, i.e. Ao & P valves]*

→ *Vice versa Diastolic murmurs are present in AR, PR & MS, TS.*

→ *THERE ARE ONLY 3 LESIONS WHICH PRODUCE A PANSYSTOLIC MURMUR ---- VSD, MR, TR*

→ *Continuous murmur is seen in --- PDA, A-V fistula, coronary sinus rupture, over large vessels*

E.C.G.



E.C.G.

PR-interval

- Measures from beginning of P wave to beginning of QRS complex.
- PR interval = PQ interval when Q is present
Represents A-V conduction time
- Duration 0.12 - 0.2 sec.
- Short PR interval is a/w Loud S₁
- In acute rheumatic fever PRi is prolonged.

ECG	Definition	Normal (seconds)	↑ in	↓ in
PRi	Beginning of Q-wave to the beginning of QRS complex	0.12 - 0.2	↓ K ⁺ , Heart block, Ac RF	
QRS	End of P-wave to beginning of ST segment			
QT	End of P-wave to end of ST segment	0.4		Digitalis toxicity
ST				

QRS duration

- Signifies mainly ventricular depolarization.
- Duration 0.08 sec-0.10 sec (but always < 0.11 sec)
- Normal direction of mean QRS vector is generally said to be -30 to +110° (from left to right)

→ Bipolar leads are standard limb leads I, II, III

→ Unipolar leads are 9

6 Unipolar chest leads (V1 - V6) precordial,

3 Unipolar augmented limb leads

(for right arm VR, left arm VL & left foot VF)

PR interval

- Time taken from start of P wave to start of R wave.
- Includes atrial depolarisation + AV node conduction + Bundle of His + Purkinje fibres.
- If this pathway is bypassed PR interval ↓es as in *WPW syndrome*. QRS complex is slurred (slurred upstroke produces delta waves or δ-waves) & QRS complex duration ↑es (wide QRS). Paroxysmal atrial tachycardia often follows an atrial premature beat.
- If this conduction bypass AV node to attach with Bundle of His resulting in pre-excitation of the ventricles, it is k/as *LGL (Lown- Ganong- Levine) syndrome*. Here PR interval ↓es but QRS complex is normal & there is no delta waves.

	WPW Syndrome	LGL Syndrome
1. PRi	↓	↓
2. QRS	Slurred (↑)	Normal
3. Delta wave	+	-

- In acute rheumatic fever there is inflammation of AV node, so PR interval ↑es but QRS complex is normal & there is no delta waves.

WPW syndrome

- Additional connecting path between atria and ventricles (**bundle of Kent**) are formed, so A-V conduction is abnormally rapid (short PR interval ≤ 0.12 sec)

Some Characteristics ECG changes

Hypokalemia and Hyperkalemia

	Hypokalemia	Hyperkalemia
○ Earliest change	Prominent <u>U wave</u>	<u>Sine wave</u> configuration
○ T-wave	Flattening & inversion	Tall, tented T-wave (peaked & narrow)
○ PR-interval	Prolonged	-
○ QRS	Wide	Wide
○ QT interval	Prolonged	↓ HR (Complete heart block or ventricular asystole may occur)
○ ST segment.	Depressed / sagging	Depressed

(PR & QRS constant when $K^+ \pm 3.5$ mEq/L)

Digitalis toxicity

- Short QT interval (d/ to rapid vent. depolarization)
- Depression of ST segment (on high dose)
- Inversion / flattening of T-wave, **inverse check mark 'v' sign present**
- Prolonged PRi (due to slow A-V conduction)
Wenckebach phenomena [2nd ° heart block, Mobitz 1]
[Remember QT Chhoti, Suppressed ST, Prolonged PR interval in digitalis toxicity]
- Depression of 'j' point (present in toxicity) distinguishes digitalis toxicity from digitalis effect.

Hypothermia

- Osborn J-wave

Acute MI

- Pathological Q-waves in transmural MI
- Inversion of T-wave & Elevation of ST-segment (in acute stage) or depression (in chronic or sub-acute stage)
- R wave amplitude ↑es in hyperacute MI. Normally the

height of R-wave progresses from V_1 to V_5 but in Acute MI this progressive ↑ is lost (poor progression of R wave).

Old MI

- Q wave present.

Heart Block

- In AV block PR-interval is > 0.2 sec.
- 3 types
 - Constant 1° → PR prolongation is seen
 - 2° (Mobitz 1 & 2) → Progressively ↑ ing PR with dropped beats
 - Complete 3° → heart block + complete A-V dissociation
- TOC
For complete HB → Pacemaker
For resistant brady unresponsive to atropine → Isoprenaline

In Acute rheumatic fever

- Sinus tachycardia
- *Non paroxysmal AV nodal* (idionodal) tachycardia.
- Prolonged PR i
- 2° heart block.

- *P pulmonale*: ↑ amplitude of P (> 2.5 mm) seen in Rt. atrial enlargement (eg. COPD)
- *M Mitrale*: ↑ duration of P = Lt. atrial enlargement (eg. MS). Bipolar p-waves are seen in V_1 .
- A short PRi + Sinus rhythm + Wide QRS is seen in WPW syndrome
- A short PRi + retrograde P waves (negative in lead II) generally indicates an ectopic pacemaker
- Esophageal leads (also k/as Lewis leads) are useful for posterior wall MI & Lt. ventricular enlargement.
- Intra-operative myocardial ischemia is best diagnosed by trans-esophageal ECHO (TEE)

CORONARY ARTERY DISEASES (CADs)

Cardiovascular Risk factors -

- Investigation of choice for cardiovascular risk : T. cholesterol / HDL.
- Predictor of CAD : HDL. ω -3 FA ↑ HDL fraction.
- CRP is a risk factor for atherosclerosis.

Non-modifiable risk factors for CAD:

- ↑ing age ,
- Having family history of heart d/s,
- Personality (type A)

Modifiable risk factors

- Smoking : Active/passive
- High blood cholesterol
- High BP
- Diabetes
- Physically inactivity
- Overweight , obesity
- Depression, social isolation and lack of quality support

AHA Recommendation to prevent IHDs:

- ↓ intake of saturated fats to <10% calories and cholesterol to <300mg/d.
- ↓ intake of saturated fats to <7% calories and cholesterol to <200mg/d in a pt with known hyperlipidemia.
- Restrict salt intake to <6 gram /d
- <30% calories from fat in diet.
- Consume variety of fruits, vegetables, fibres etc.

ANGINA PECTORIS

(Non-infarct effect of myocardial ischemia)

- Paroxysmal pain in substernal/precordial region of chest.
- Often pain radiates to left arm, neck, jaw.

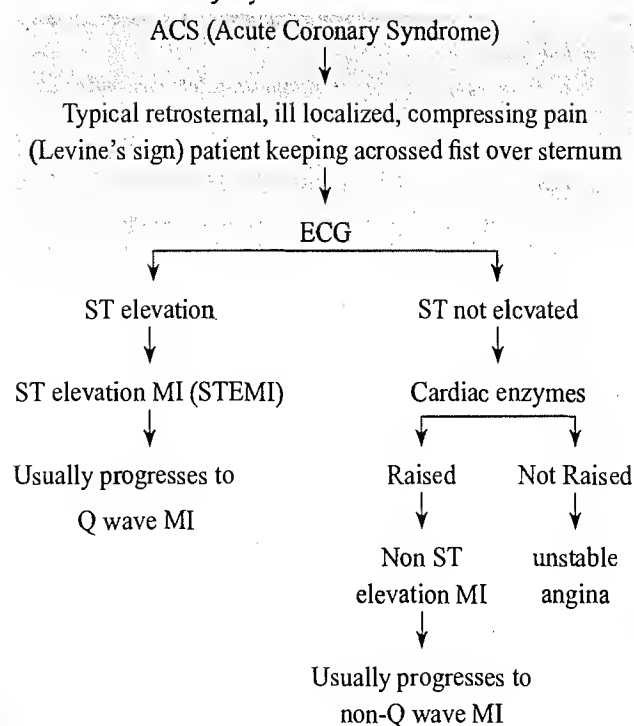
Feature	Classic / stable angina	Prinzmetal's/ variant angina	Unstable / crescendo angina
Occurrence	M/c form	Uncommon	
Relation with physical activity	+	No	At rest or accelerating angina
Relieved by	Rest	Not so	
Preceder	Arteriosclerosis	Vasospasm (transmural/ total ischemia)	Micro-infarction/ Pre-infarction angina
Followed by	Crunch during diastole	MI is exceptional	Forerunner of MI
ECG	ST depression	Transient elevation of ST, Hyperacute T-wave	
T/t		Nifedipine, Diltiazem	Heparin ↓ Oral aspirin
Contra/I		Propanolol	Avoid anti-arrhythmics

Transmural MI (STEMI)

3 stages

- Hyperacute stage --- ST elevation, large T wave
- Evolving phase --- Q wave may appear, T-wave starts inverting, ST -starts settling
- Fully evolved --- T-wave everted or gone back to normal
- Old MI --- Q-waves only

Acute coronary syndrome



MYOCARDIAL INFARCTION - Types

	Anterior - wall MI	Inferior wall MI	Septal MI
Most	Common	Serious	Rare
Artery involved	LAD	RCA	
ECG	ST-elevation in V ₁ -V ₆ (esp V ₃), Q-waves in lead V ₁ through V ₄	Q-waves in lead II, III, aVF	Changes in lead V ₁ -V ₄
A/w	Mural thrombosis, sympathetic stimulation	Rt ventricular infarction, Parasympathetic stimulation	Both systemic & pulmonary embolism
T/t		Give IV-fluids	

- Time after acute MI when cardiac muscle is most subjected to rupture -- b/n 3 to 7 days when the muscle is softest.
- Commonest complication of acute MI ---
Arrhythmias (ventricular extrasystoles) > LVF > cardiogenic shock > Cardiac rupture.
- M/c late complication of acute MI --- Ventricular aneurysm (persistent 'ST elevation' on ECG is suggestive)
- M/c cause of death in acute MI --- VT leading to VF & death
- Pathological Q-wave are indicative of myocardial necrosis (old MI)
- All MI produce ST-elevation except subendocardial MI in which ST depression is seen.
ST elevation is a manifestation of transmural or subendocardial ischemia.
- ECG is least sensitive in diagnosing left circumflex a. infarcts.
- Commonest vessel thrombosed in acute MI -- LAD > RCA > LCx.
- Indications of PCTA --- angina refractory to medical t/t, single vessel ds, proximal non calcified stenosis, prior bypass surgery.
- Propranolol is contraindicated in Prinzmetal's angina.
- Most of the deaths after a MI are seen within the first one hour.
- M/c valvular heart lesion after MI --- MR.
- Best marker for stratification of cardiovascular risk is --- High sensitivity C-reactive protein (hs CRP).
- BNP is a cardiac marker (Best for CCF).
- M/c cause of death after thrombolytic therapy --- Reperfusion arrhythmia.

T/t of MI

- Aspirin - in all cases unless contraindicated
- Thrombolytic therapy:
 - Useful in <12 hrs, ST segment elevation, enzymes +
 - Absolute c/ind:
 - Hemorrhagic stroke
 - Ischemic stroke within 1 yr
 - BP ≥ 180/110
 - Suspected aortic dissection
 - M/c cause of death after thrombolytic t/t : Reperfusion arrhythmias.

- Most feared c/c of thrombolytic/ fibrinolytic therapy is --- Intracranial hemorrhage
- Thrombolytic/ fibrinolytic therapy is not indicated in --- UA/ NSTEMI
- Streptokinase and urokinase are contraindicated in --- Hemorrhagic stroke, suspected aortic dissection, severe hypertension (BP > 180/110), aneurysm

Agents:

	Agents	Peculiarities
1. Infusion form	Streptokinase	Obtained from β hemolytic streptococci, Works in organised thrombus (>4hr), causes less chances of h'age in elderly
	Urokinase	Obtained from human urine
	Alteplase (r tPA)	Recombinant
2. Can be given as i/v bolus directly	Retenapase	Recombinant
	Tenecteplase	Longest acting

- Last 3 i.e. alteplase, reteplase and tenecteplase are more potent, so they are preferred.
- **Alfemprase** is a metalloproteinase that degrades fibrin/ FI
- EACA & Tranexemic acids are specific antidotes for overdose of fibrinolytic agents.
- β-Blockers:
 - Decrease myocardial oxygen demand. Work as prophylaxis for arrhythmias.
 - C/ind:
 - AV block
 - HR <60/min
 - Obstructive airway d/s (asthma)
 - PVD (risk of gangrene).
- Calcium channel Blockers (CCB's):
 - Used only when β-blockers are contraindicated
 - Diltiazem & verapamil are used. DHP's (nifedipine) is not used.

HEART SOUNDS

S2 : Second heart sound

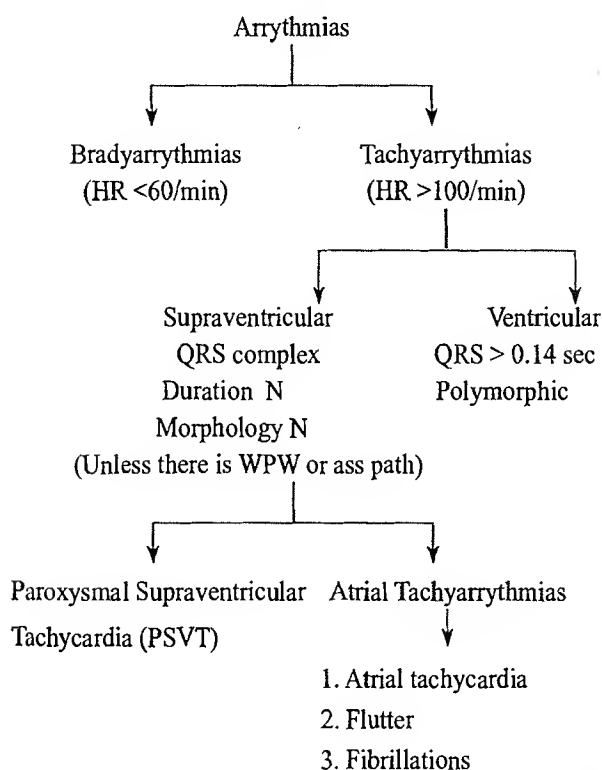
- Due to closure of semilunar valves (aortic & pulmonary).
- Normally A2 is followed by P2.
- In inspiration blood ↑ ses in RV but ↓ ses in LV. So split of S2 ↑ ses. In Expiration blood ↓ ses in RV but ↑ ses in LV. So split of S2 ↓ ses.

S1 ---- A2---- P2

Split of S2:

Wide Split		Paradoxical split	
Variable		Fixed	Pattern is S1 ---P2---A2
Inspiration & expiration split diff.			
Early A2	Late P2	Early P2	Late A2
VSD, MR, LV ectopic, LV pacemaker	RBBB, PS	ASD	Bundle of Kent (accessory paths which takes impulse earlier to RV) LBBB, AS, Systemic HTN

Atrial CARDIAC ARRHYTHMIAS



SUPRAVENTRICULAR TACHYARRTHMIAS

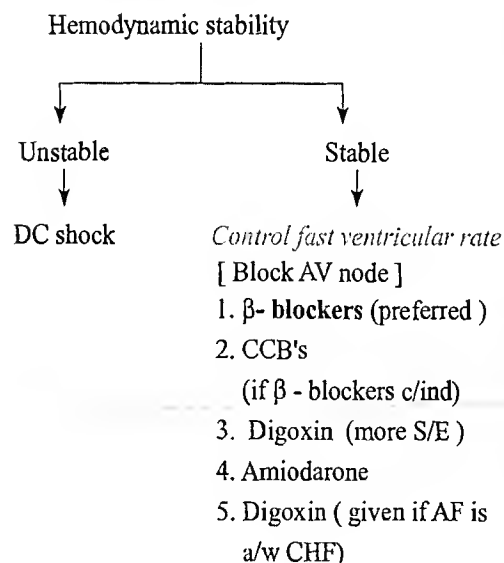
PSVT

- Normal wave is f/b QRS complexes but no P wave becoz P wave is merged into QRS complexes.
- ECG : **P wave absent**, R-R interval ↓ se or constant (regular). QRS morphology is normal.

AF (Atrial Fibrillations)

- Rate is >350/min.
- R-R interval irregular & variable.
- QRS morphology is normal.

T/t :



Convert AF into sinus rhythm

- DC cardioversion
(Always rule out atrial thrombus first)
- Ibutilide
(k/as medical defibrillator)

Maintenance of sinus rhythm

- Amiodarone
- Sotalol
(if a/w CAD)

T/t of AF + WPW syndrome

If drugs given to control fast ventricular rate, then conduction ↑ ses through accessory pathway. So to block both → **Flecainide/procainamide/ibutilide** can be used.

VENTRICULAR TACHYARRTHMIAS

	Definition	Pattern on ECG	T/t
1. Ventricular tachycardia (VT)	>3 consecutive ventricular ectopia at HR >100/min		1. Non-sustained treat underlying cause (Amiodarone, ibutilide) 2. Sustained or polymorphic : treat like VF or VFI see below
2. Ventricular flutter (VF)	HR >250/min	Only QRS, No other wave	DC cardioversion + i/v lignocaine
2. Ventricular fibrillation (VFI)	---	Chaotic pattern	F/b amiodarone maintenance

VT (Ventricular Tachycardia)

Monomorphic

- Origin from single focus of myocardium.
- QRS have same morphology

Polymorphic VT

- Also k/as *Torsades de pointes*.
- Mainly d/to drugs : Sevoflurane, terfenadine
- Hallmark is prolonged QTc ($> 460-480$ ms). Resting bradycardia (HR < 60) may be seen.
- Can lead to ventricular fibrillation & sudden death (SIDS).

Congenital Long QT Syndrome

- Also k/as *Romano Ward syndrome*
- It is an **AD** disorder which usually presents with **syncope** during childhood or adolescence. Syncope may be precipitated by sympathetic stimulation, exercise or fright.
- It is d/to recurrent bouts of rapid polymorphic VT k/as **Torsade de pointes**
- Hallmark is prolonged QTc ($> 460-480$ ms). Resting bradycardia (HR < 60 may be seen)
- C/c : Sudden death (SIDS)

Acquired Long QT Syndrome

May be seen with drugs e.g. droperidol, quinidine, TCA; metabolic disorders or SAH, right radical neck dissection

Sick Sinus Syndrome

- Common cause of **bradycardia** which may contribute to CHF.
- SA node is depressed and is vulnerable to external influences e.g. vagal stimulation and certain drugs
- Many patients are asymptomatic, although syncope and palpitations are often described
- C/c : Sudden death (SIDS)
- T/t : Atria based pacemakers

HEART BLOCK

Disturbance in the transmission of impulses generated in SAN. 3 types

- SAN block
- AV block (block at the level of AVN)

- BBB which has further 2 types RBBB and LBBB

SAN block

Rhythm is not generated at the level of SA node and hence whole heart beat is lost initially but after approximately 2 cardiac cycles, other pacemaker take over this function.

AV Block

- Conduction from atria to ventricles is lost.
- Types:

1. Incomplete heart block : D/to partial disturbances in conduction. It is of 2 types

(a) *First degree AV block* : All atrial impulses reach the ventricle but PRi is abnormally prolonged.

- A:V rate is 1:1
- PR is abnormally prolonged (> 0.20 sec)
- Seen in digitalis toxicity, b-blockers, CCB

(b) *Second degree AV block* : All impulses do not reach the ventricle. So also k/as intermittent AV block

- A:V rate is 2:1 or 3:1
- PR is abnormally prolonged (> 0.2 sec)
- Two types

Mobiz type 1 (Wenckebach block)	Mobiz type 2
Gradual lengthening of PRi, normal QRS	Normal PRi but QRS widening
Seen in digitalis toxicity, β -blockers, sometimes also with CCB	Seen in conduction defects Of His Purkinje system
Seen transiently in inferior wall MI	

	Mech	Cause	Site of block	ECG, T/t
1 ⁰	Slow conduction from A \rightarrow V	β -Blocker, CCB's Digoxin	AVN	PRi prolonged
2 ⁰	Intermittent failure of conduction	Mobiz-I Digoxin	AVN	Progressive \uparrow se in PRi (Wenckebach phenomena)
		Mobiz-II	Bundle of His	Sudden drop beat without any PRi prolonga ⁿ Require pacemaker
3 ⁰	Complete failure of conduction	MI	AV dissociat ⁿ	Require pacemaker

2. Complete heart block (3rd degree block):

D/t to complete loss in conduction b/w atria and ventricles. Therefore ventricles beat with a much slower rate (**idioventricular rhythm**)

- If it develops suddenly --- dizziness and fainting may result (*Stokes Adams syndrome*)
- Seen in digitalis toxicity, MI
- T/t : pacemaker.

→ Digoxin does NOT cause Mobitz type 2 block.

→ Hypothyroidism is a/w increased level of --- Cholesterol

Bundle Branch block (BBB)

- Block in the one of the branches of bundle of His
- Characterised by normal HR, prolongation of QRS, abnormal ST and T, split S2
- It is of 2 types
 1. **RBBB** : RV contracts after LV
 2. **LBBB** : LV contracts after RV block can also occur in anterior or posterior fascicular branches. It is also k/as hemiblock or fascicular block.
 - (a) Left anterior hemiblock : Abnormal left axis deviation
 - (b) Left posterior hemiblock : Abnormal right axis deviation in ECG.

Coarctation of aorta (CoA)

- Defect lies in tunica media of aorta.
- Can occur anywhere from transverse arch to iliac bifurcation.
- M/c site : Juxtaductal (distal to origin of Lt. subclavian artery) near the insertion of ligamentum arteriosum which is at origin of ductus)
- CoA is m/c heart d/s in a pt of **TURNER SYNDROME**
- Associations —**
 - Subaortic stenosis, **bicuspid aortic valve** (most commonly) congenital MS. (*Coarctation syndrome*)
 - CoA is a/w Lt. Sided obstructive lesions: "Shone complex"
- More common in males
- Hypertension is marked in arteries proximal to coarctation (*headache, epistaxis, dizziness*) — UL
- Weakness, pain in legs following exercise (intermittent claudication), absent pulses in LL
- M/c surgical cause of diastolic HTN
- Signs - radio femoral delay

BP in UL > LL (normally BP in LL > UL by 10-20 mm Hg)

- CoA leads to LVH and HTN, pulmonary congestion (*dyspnea*)

On CXR

Notching of inferior border of ribs (4th-8th) d/t erosion by enlarged collaterals

Inverted sign on Ba- studies (figure of 3 sign), LVH

C/c

Aneurysm of descending aorta,

Rupture of Berry aneurysm → ICH

Renal ischemia → diastolic HTN

- T/t --- Surgical repair and reanastomosis is TOC
- PGE₁ infusion in symptomatic neonates

HOCM

- Secondary to obstructive congenital heart lesions (critical AS, CoA) or d/t type 2 glycogen storage d/s (Pompes).
 - HCM also occurs in infants of diabetic mother (with or without obstruction) which regresses itself.
 - HCM also seen in premature infants receiving corticosteroids for chronic lung disease it resolves with cessation of steroid therapy.
 - Most cases are inherited as AD mode (chromosome 14)
 - H/O sudden death in family.
 - Symptoms:-**
 - Atypical angina : frequent chest pains at rest, exercise syncope, CHF d/t diastolic stiffness. Systolic function is normal
 - Signs:-** Carotid upstrokes (with spikes & dome character), graying out spells, typical murmur.
 - Double / triple apical impulse, S4 sound is audible.**
 - Patho:-**
 - Asymmetrical hypertrophy of septum + Systolic anterior motion of anterior leaflet of mitral valve.
- ↓
- Both produce dynamic obstruction of LV
 - Banana shaped cavity*
 - [Extensive myocyte hypertrophy with myofibre disarray on microscopy]
 - T/t : β-blockers (Propranolol) are mainstay of t/t. CCB, amiodarone may be given for arrhythmia. Surgery is septal artery embolization.
 - Drugs contra indicated are - 3d digoxin, diuretics, vasodilators, i.e. drugs that ↓ ventricular size or ↑ contractility.*

• Murmur of HOCM

It is a ESM (ejection systolic murmur) heard along LSB with no radiation to neck. Diamond shaped crescendo - decrescendo murmur. Murmur decreases on ↑ in blood flow.

• Murmur of HOCM is ↑ by [3 'D']

- Contractility ↑ se : Digitalis, isoprenaline
- Preload ↓ se : diuretics, Valsalva manoeuvre, standing all which ↓ se venous return,
- Afterload ↓ se : Vasodilation (Inhalation of amyl nitrite, nitrates)

• Murmur of HOCM is ↓ by

Phenylephrine, hand grip exercise, leg raising, squatting, lying down (actions that ↑ se cardiac size by ↑ ing VR)

FACTORS AFFECTING OTHER MURMURS

Factor	Effect
Respiratory variation	Inspiration : Rt sided murmur ↑ se Expiration : Lt sided murmur ↑ se
Valsalva	+ve intrathoracic pressure : All murmurs ↓ se
Drugs	Amyl nitrate : BP ↓ se → murmurs of AR ↓ se (AS ↑ se) Phenylephrine : BP ↑ se → murmurs of AR ↑ se (AS ↓ se)
Postural	Standing : All ↓ se except HOCM Squatting : All ↑ se except HOCM

→ HOCM is exception

→ The only murmur which ↑ se in intensity on valsalva manoeuvre
--- Murmur of MVP

→ HOCM is a cause of sudden death.

→ M/c cardiomyopathy is dilated CM.

→ Doxorubicin induced CMP is dilated type.

→ Previous viral myocarditis is common cause for DCM.

→ M/c cause of death in HOCM is - Sudden cardiac death secondary to ventricular tachycardia.

→ Sudden cardiac death may occur in - CAD (m/c cause), HOCM, Eisenmenger's syndrome, AS, MVP, Long QT syndrome etc.

DCM and restrictive Cardiomyopathy

Point	DCM	RCM
Occurrence	M/c	Less
Risk factors	Reversible Alcoholism, peri-partum, hypocacemic, Toxins Co, Hg, Pb & Se-deficiency, thyroid disorder, acromegaly, cocaine abuse, chronic uncontrolled tachy	Infiltrative ds (like amyloidosis, <u>hemo</u> chromatosis, sarcoidosis, carcinoid synd, <u>endo</u> myo <u>fibro</u> elastosis, Pompe's ds., idiopathic eosinophilia)
	Irreversible NAXO's d/s Thrombus in RV DM, Drugs (doxorubicin, imatinib, trastuzumab, cyclophosphamide) Autoimmune (SLE, RA) Thiamine deficiency, Duchene's MD	
Dysfunction	↓ in contractile function of left, right or both ventricles	Myocardium becomes stiff, <i>Systolic function normal in early stages</i>
CXR		Signs of pulmonary hypertension
T/t	ACEi	Diuretics

RHEUMATIC FEVER (RF)

- RF is caused by β-hemolytic streptococci group A
- Cross reaction b/w exogenous antigen (epitope) and the host is seen. Antibodies directed against M proteins of streptococci cross react with tissue glycoproteins in the heart, joints, and other tissues.
- Occurs in about only 3% of patients with group A streptococcal pharyngitis/ sore throat.
- Affects children between 5-15 years age.
- Jones criteria of RF

Major Criteria	Minor Criteria	Essential criteria
1. Carditis	(A) Clinical	<i>Evidence of strept infection</i>
2. Polyarthrititis	(i) fever	(a) Increased ASO titre
3. S.C. nodules	(ii) Arthralgia	(b) Positive throat culture
4. Chorea	(iii) Previous RF or RHD	(c) Recent scarlet fever
	(B) Laboratory	
	(i) Acute phase reactant, leucocytosis elevated ESR, CRP	
	(ii) Prolonged PR interval in ECG.	

To fulfill the Jones criteria either two major criteria or one major criterion and two minor criteria + evidence of antecedent streptococcal infection are required.

- Aschoff bodies are pathognomonic for RF. Aschoff's bodies or nodules are composed mainly of T-lymphocytes and also of plasma cells, plump macrophages, **antischow cells** admixed in eosinophilic collagen.

Pathological manifestations of Acute RF

	Features
Endocardium	Valvular : Vegetations (firm, warty) along the line of closure, Aschoff's bodies
	Mural : MacCallum's patch (in left atria), Aschoff's bodies
Myocardium	Aschoff's bodies
Pericardium	Serofibrinous pericarditis (Bread & butter type)

- Carditis seen in RF is pancarditis, can involve any layer of heart. Starts from endocardium & valves → myocardium → pericardium. Myocarditis can cause cardiac dilation that may evolve functional MR or even heart failure.

[**Remember** : that constrictive pericarditis is NOT seen in acute RF].

LATE MANIFESTATIONS OF RF

1. Sydenham's Chorea

- Develops after 3 months of onset of acute RF), more common in females.
- Purposeless jerky movements, resulting in deranged speech, m/s incoordination, awkward gait and weakness seen in emotionally disturbed child.
- Self limiting course.

2. Subcutaneous nodules

- Appear on bony prominences like elbow, shin, occiput and spine.
- Non tender, pinhead to almond sized.

→ Early manifestations are carditis, arthritis, erythema marginatum

→ Arthritis is m/c manifestation in adults.

→ Valvular damage is the hallmark of carditis.

→ Revised Jones criteria does NOT include -- ↑ TLC, fever in minor criteria

→ In rheumatic carditis early valve replacement will ameliorate CCF.

MVP / Barlow's syndrome -

- One or both mitral valve leaflets are floppy and prolapse or balloon back (abnormal displacement) into left atrium during systole.
- Histologically there is **myxomatous degeneration** in the valve.
- More common in females. Most of the time patient remains asymptomatic.
- CI/F: Atypical chest pain (non-exertional & transient), palpitation, dyspnea & fatigue.
- O/E -

Characteristic **mid-systolic clicks** which are multiple; Late systolic murmur. Murmur ↑ & click is louder on standing, after sublingual GTN, with tachycardia, straining phase of Valsalva maneuver.

ECG normal

M-mode ECHO : late systolic sagging / motion of the posterior, ant. or both leaflets

- Sudden death may occur.

Cardiac tamponade vs Constrictive pericarditis

	Cardiac Tamponade	Constrictive Pericarditis
Mechanism	↑ intrapericardial pressure ↓ Impaired diastolic filling of ventricles	
Pulsus paradoxus	+	Usually -nt
Pericardial effusion on echo	+	-
Most sensitive finding,	Rt atrial collapse	
Most specific	RV collapse	
Prominent descent	X	Y descent
Electrical alternans	+	
ECG	↓ Amplitude of QRS	<u>Square root sign</u> on ventricular tracing
Kussmaul's sign	+/- when present suggests epicardial constriction	+

GIT

Chronic Gastritis

Type A (Body predominant)

1. Auto immune chronic atrophic gastritis
2. Caused by anti parietal cell antibodies, (Vit B₁₂ malabsorption/ pernicious anemia is seen)
3. A/w hypoparathyroidism, Addison's ds, vitiligo
4. Lab/f: ↑ Serum gastrin, ↓ Gastric acid secretion (hypo-/ achlorhydria)

Type B (Antral predominant)

1. Is environmental gastritis
2. Serum gastrin is often normal

Gastritis

→ *Reflux gastritis* is seen after gastric surgery, caused by entero-gastric reflex.

→ *Antral gastritis* is commonly seen d/to NSAIDs & alcohol.

→ *Atrophic gastritis* is d/to H.pylori, NSAIDs.

Blind Loop Syndrome

- Also k/as **bacterial over growth syndrome/stagnant bowel syndrome**.
- Comprise group of disorders with diarrhea, steatorrhea and macrocytic anemia.
- There is proliferation of colon-type bacteria (E-coli/ bacteroids) within the SI d/to impaired peristalsis (functional / anatomical stasis) or direct communication between the small and large intestines.
- Anatomical stasis may be d/to diverticula, fistula/ strictures related to Crohn's disease, surgeries. Functional stasis may be seen in scleroderma.
- In general high loops produce steatorrhea (d/to fat malabsorption), & whereas low loops tend to produce anemia (d/to vit B₁₂ deficiency secondary to binding of the vitamin by anaerobic bacteria).
- D/g**: ↓ Serum cobalamin + ↑ folate level. Abnormal Schilling test which normalizes after 5 days tetracycline t/t. ¹⁴C-D-Xylose breath test
T/t: Mainly surgical extirpation (TOC). Broad spectrum antibiotics (for functional stasis)

→ Normal concentration of bacteria in small intestine is about 10⁵/ml

Small Bowel (Short Bowel) syndrome

- Develops after extensive resection of the small bowel intestine (trauma, mesenteric thrombosis, regional enteritis, radiation enteropathy, strangulation) M/c pediatric causes are NEC and congenital atresias.
- CI/f** - depends upon extent & resection site --- when small intestine remains <3 meter serious nutritional problems develop.
- If the proximal SI (*jejunum*) is resected, the ileum is able to take over most of its absorptive function.
- If distal small bowel (*ileum*) is resected ≥ 1.2 m: Produces greater degree of malabsorption than removal of complete length of proximal SI. Bile salts malabsorption occurs (steatorrhea and diarrhea results, which is more pronounced if ileocecal valve is resected & blind loop synd. may develop) and cobalamin or **Vit. B₁₂ deficiency**.
- In **extensive ileal resection** with intact colon calcium oxalate urinary calculi develop (enteric hyperoxaluria). Hypercalcemia and hypercalciurea may leads to renal stones.
- Gastric hypersecretion (esp. after proximal resection) b/of loss of inhibitory hormones normally secreted by SI.
- Lab/F** — ↑ Basal and post prandial serum gastrin levels.
- T/t** — TPN for 1-3 months & Vitamin B₁₂.

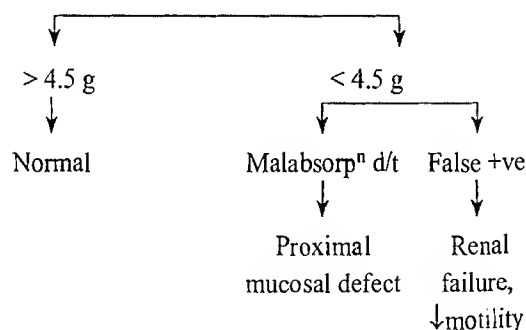
MALABSORPTION

Fat/lipid malabsorption

Steatorrhea: M/c manifestation of malabsorption syndrome is steatorrhea, which is 72 hr fecal fat estimation >6 gm% (an ↑ in fecal fat >6% of dietary intake)

Carbohydrate malabsorption

D-Xylose test: It distinguish pancreatic cause from intestinal cause. 25 µg of D-xylose is given & concentration in 5 hr urine sample is analyzed

Vit B₁₂ malabsorption

Schilling test can localise the site of malabsorption. Radiolabelled cobalamin (⁵⁸Co) is given and its levels are measured in 24 hr urine. If it is <10% then proceed step2.

D/s	<10%	>10% excretion is seen in
1. Normal	Proceed with step 2	Normal
2. Add IF	N	Pernicious anemia
3. Add pancreatic enzymes	N	Chronic pancreatitis
4. Add antibiotics for 5 days	Ileal d/s, Crohn's, tropical sprue, ileocaecal TB	Bacterial overgrowth syndrome

- *Bentiromide test* is used for exocrine pancreatic insufficiency.
- Giardiasis is m/c infection implicated in malabsorption.
- Intrinsic factor of Castle is secreted by parietal cells of the fundus/body of stomach.
- IOC for GERD is 24 hr pH manometry.

LIVER

Portal Hypertension

		Example
○ Pre-sinusoidal	Extra-hepatic	Portal vein thrombosis, Massive splenomegaly
	Intra - hepatic	Portal tract fibrosis (NCPF), Schistosomiasis, Vinyl chloride, Caroli's d/s
○ Sinusoidal		Cirrhosis
○ Post-sinusoidal	Intra - hepatic	Veno-occlusive d/s
	Extra - hepatic (Hepatic vein/ IVC)	Classic Budd chiari syndrome

NCPF (Non Cirrhotic Portal Fibrosis)

- Pre-sinusoidal intrahepatic fibrosis of portal tract.
- Hallmark of the d/s is thrombosis/sclerosis of the portal vein branches (major branches level 1,2) → formation of mesangiosinusoids/ periportal cavernoma.
- Portal venopathy leads to esophageal varices and recurrent UGI bleed.
- Affects males 20-30 yrs
- **Positive findings:**
 1. Splenomegaly massive
 2. Malarial Ag+
 3. Hepatitis B Ag+
 4. Hematemesis

Negative findings:

There is no ascites, encephalopathy, jaundice or malnutrition.

- Hepatic vein wedge pressure is N/ ↑.

EHPO (Extra hepatic portal venous obstruction)

- M/c cause of portal HTN in children <10 yr (1st-2nd decade).
- Portal vein branches (smaller branches level 3,4) →
- Affects 10-20 yrs.
- **Positive findings:**
 1. Splenomegaly massive
 2. Recurrent UGI bleed +
 3. Malena, anemia
- Hepatic vein wedge pressure is low.

Auto-antibodies in Hepatitis

Features	Positive in
Anti-actin, Atypical pANCA	Type I autoimmune hepatitis
Anti LKM-1	Type II autoimmune hepatitis
Anti LKM-2	Drug induced hepatitis
Anti LKM3	Chronic hepatitis D

Auto-immune Hepatitis

Type	Type I	Type IIa	Type IIb	Type III
Sex	Young females	Young females	Elderly males	Young females
Scrology	ANA +	anti-LKM-1	Hcp C +ve	Liver soluble Ag-Ab
Recurrent jaundice	+	+	+	+
T/t	Steroids	Steroids	INF	Steroids

T/t of Hepatitis

Type	T/t
Chronic Hepatitis B	IFN-α, Lamivudine, adcofovir, entecavir
Chronic Hepatitis C	PEG IFN-α + ribavarin
Chronic Hepatitis D	PEG IFN-α
Autoimmune	Prednisolone, azathioprine
Cryptogenic	? steroids

Complications of Hepatitis

C/c	A	B	C	D	E
1. Fulminant hepatitis	0.1%	0.1%	0.1 - 1%	5% (co), 20% (super)	↓
2. Chronicity	0 %	1-10%	70-80%	Variable	0%
3. Carrier	x	more	less	Variable	x
4. Cancer	x	more	less	Variable	x
5. Cholestasis	+	-	-	-	+
6. EMC	-	-	+	-	-
7. MPGN	-	++	+	-	-
8. MGN, FSGS	-	+	-	-	-

[EMC Essential mixed cryoglobulinemia]

- Fulminant rate are max^m in superinfection of hepatitis D.
- Maternal mortality is highest with fulminant hepatitis E in pregnancy.
- Marker for carcinoma is HBx Ag.
- Marker during window period: IgM Anti HBc.
- Markers for HBV replication:
 - Quantitative marker → HBV-DNA, DNA polymerase.
 - Qualitative marker → HBeAg.
- Post vaccination serology is done by HBs Ag.
- Sulfonamide may cause acute fatty liver & cholestatic jaundice.

Chronic hepatitis

- Chronic persistent hepatitis: Low infectivity +, HBeAg -, HBsAg+, IgM HBc- , HBV-DNA +
- Chronic active hepatitis: (High infectivity, HBeAg + chronic hepatitis): HBeAg+, HBsAg+, IgM HBc- , IgG Anti-HBc +, HBV-DNA +

Hepatic Encephalopathy

○ Precipitating factors:

- GI hemorrhage.
- Infections: Spontaneous bacterial peritonitis and pneumonia may present with HE.
- Renal and electrolyte disturbances. Renal failure, metabolic alkalosis, hypokalemia, dehydration, and diuretic effects.
- Use of psychoactive drugs. This factor may require a urine screen for benzodiazepines, narcotics, & other sedatives.

5. Constipation

6. Excessive dietary protein.

7. Acute deterioration of liver function in cirrhosis.

○ Triphasic waves are seen in stage 2.

○ T/t:

- Lactulose is a first-line pharmacological treatment of HE.
- Bowel cleansing → reduction in nitrogen load is a standard therapeutic measure in HE.
- Ornithine aspartate
- Neomycin , metronidazole
- Flumazenil and bromocriptine administration may have a therapeutic role in selected patients.

KIDNEY AND GUT

Renal failure indices in ARF

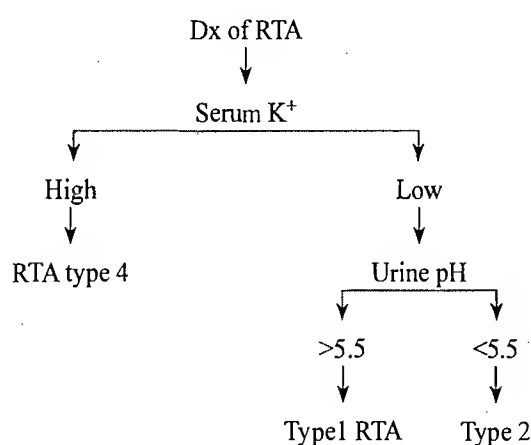
Diagnostic index	Prerenal Azotemia	Intrinsic Renal failure (ATN)
1. Fractional excretion of Na ⁺ $FeNa = \frac{(U_{Na} \times P_{Cr} \times 100)}{(P_{Na} \times U_{Cr})}$	< 1	> 1
2. Urinary Na ⁺ (mmol/L)	< 10	> 20
3. U _{Cr} : P _{Cr} ratio	> 40	< 20
4. Urine specific gravity	> 1.020	~ 1.010
5. Urine osmolality	> 500	< 350 (~ 300)
6. Plasma BUN/Cr ratio	> 20	< 10-15
7. Renal failure index $U_{Na} : U_{Cr} / P_{Cr}$	< 1	> 1
8. Urinary sediments (casts)	Hyaline	Muddy brown cast

- Fractional excretion of sodium (FeNa) is most useful to differentiate prerenal from intrinsic RF.
- Oliguria, Hypocalcemia & ↑ BUN are found in early phase of ARF
- Hypervolemic hyponatremia is seen in renal failure.
- High BUN/Cr ratio (20:1) or a disproportionate less ↑ in Cr is seen in pre-renal failure.

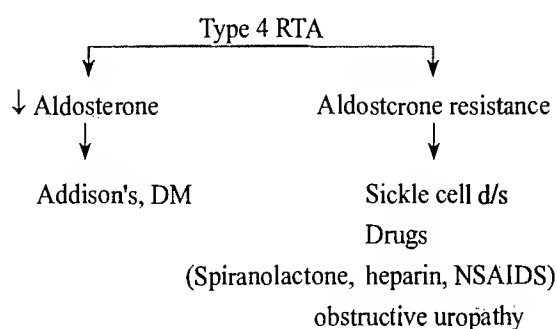
Renal Tubular Acidosis (RTA)

- RTA is a disorder of renal acidification out of proportion to ↓se in GFR.
- Hyperchloremic *normal anion-gap metabolic acidosis* is seen d/to ↓se H^+ excretion from α -intercalated cell (in RTA type 1) & bicarbonaturia (type 2).
- 4 types of RTA exist. Type 1 is distal RTA and type II is proximal.
- Type 1 & 2 are differentiated by urinary pH while type 4 is differentiated from other types by serum K^+ levels.

Diagnostic Algorithm



- RTA type 4 is always acquired. 2 mechanisms are there



$\uparrow H^+$ from absorption → leads to metabolic acidosis
 \downarrow Excretion by principal cells → leads to $\uparrow K^+$
 $\uparrow H^+$ from α -intercalated cells → urine pH <5.5

- In type 1 RTA kidney is able to acidify urine during spontaneous or NH_4Cl induced acidosis (urinary pH > 5.5 in type 1). This ability is lost in type 2 RTA.
- Correction of acidosis with HCO_3^- will result in bicarbonaturia in type 2 RTA but not in type 1 RTA.
- Lead (Pb) causes RTA type II (proximal RTA)

Differentiating points:

- In diarrhoea, Type 1 and 2 RTA --- Hypokalemic acidosis but in type 4 there is hyperkalemic acidosis
- In diarrhoea there is GI loss of HCO_3^- Urine AG is -ve, urine pH is 5-6, serum K^+ may be low, daily acid excreⁿ ↑high.

	Type I (Distal)	Type 2 (Proximal)	Type 4 (Hyperkalemic)
Urine pH	> 5.5	< 5.5	< 5.5
Urine AG	+	+	+
Serum K^+	↓	↓	↑
Daily acid excre ⁿ (citrate)	↓	N, or ↑	↓
Fractional HCO_3^- excr ⁿ	< 10%	> 15%	< 10%
Causes	VDDR, Galactosemia, sickle cell d/s, Sjogren's syndrome, Li, AMB, Lead	MM, Cystinosis Fanconi syndrome, GSD's, Wilson's d/s Acquired : Lead	DM, chronic interstitial nephritis, spironolactone, Heparin, NSAIDS, SCD, obstructive uropathy
Mech	↓ K^+ absorp ⁿ from distal α -intercalated cells ↓ Hypokalemia	↓ K^+ absorp ⁿ from PT ↓ Hypokalemia, bicarbonaturia, aminoaciduria, glycosuria phosphaturia	↓ K^+ excretion from principal cells ↓ Hyperkalemia, Hyporeninemic hypo- aldosteronism
Cl/f	↓ urinary citrate, hypercalcemia ↓ Nephrocalcinosis M/s weakness, Polyuria, skeletal deformity	FTT renal osteodystrophy nephrogenic DI	↑ susceptibility to hyperkalemia with drugs (ACEI & NSAIDS)
R _x	$NaHCO_3$ tab, alkali t/t Shoals solution	alkali t/t, thiazides, K^+	

Interstitial Nephritis

- Salt losing nephropathy* seen
- M/c dg causing I~ : Methicillin (Allopurinol, cephalothin also involved)
- Eosinophilluria* is seen in antibiotic induced allergic interstitial nephritis and atheroembolic ARF.

CRF (Uremia)

- "Half and half nail sign" with a white proximal and red distal half of nail bed, is seen in CRF patients (Azotemic onychopathy)
- Electrolyte abnormalities: $\uparrow K^+$, H^+ , BUN, PO_4 , $\downarrow Ca^{++}$ and \uparrow or $\downarrow Na^+$, Metabolic acidosis. Very rarely $\downarrow K^+$
- A disproportionate elevation of blood urea as compared to serum creatinine occurs in pre-renal azotemia.
- There is compensatory dilatation of surviving neurons.
- A definitive diagnosis of CRF can be established on the basis of bilaterally reduced renal size.
- Restless leg syndrome is seen in uremia and it is treated by L-dopa and ropinirole
- Hemodialysis can correct HTN, pulm. edema, hyperkalemia, pericarditis, encephalopathy. Hemodialysis can not revert back infertility, osteodystrophy and anemia.
- Role of EPO (erythropoietin) in t/t.

Barter & Gitelman Syndromes

C/F	Barter syndrome	Gitelman syndrome
Mutation of	$Na^+K^+2Cl^-$	$NaCl$
Hyperaldosteronism	2^0	2^0
Na^+ loss	Severe	Mild
Presentation	May be in fetal life, Oligohydramnios	Late after birth
C/F	Polyuria, polydipsia, recurrent episode of dehydration, cramps, weakness, Deafness	
Prostaglandins	\uparrow	N
Role of NSAID	+	-
S. Ca^{++}	\downarrow	\uparrow
S. Mg^{++}	\downarrow	$\uparrow\uparrow$
S. K^{++}	\downarrow	\downarrow
S. Na^+	N	N
Remark	Furosemide can lead to Barter syndrome	Thiazides can lead to Gitelman syndrome

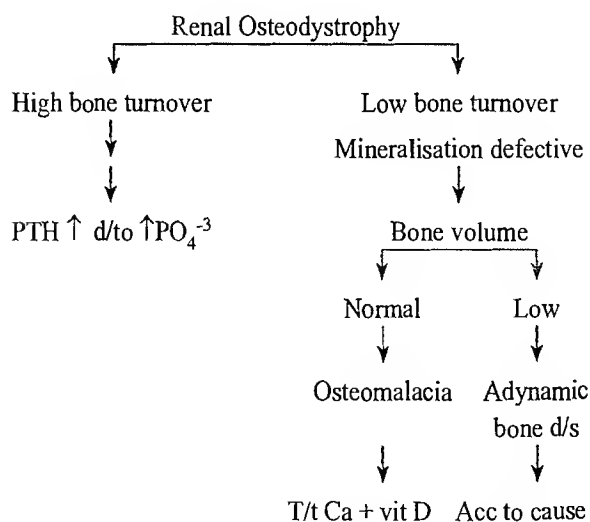
→ Na^+ activating mutations can lead to Liddle syndrome and 1^0 hyperaldosteronism.

Renovascular Hypertension

- Screening test of choice : MR angio
- Gold standard or conventional method for diagnosis : Renal angiography/ arteriography.

Renal osteodystrophy

- Disorders of calcium, phosphorus, & bone in CRF are collectively k/ as R~.
- In CRF excretion of phosphorus is impaired leading to hyperphosphatemia. Excess phosphate binds to calcium & causes hypocalcemia → stimulation of PTH → secondary hyperparathyroidism. which in turn normalizes serum P
- Lab/f --- Serum Ca low or N, Serum P High or N
- X-ray spine --- "Rugor jersey spine" is seen d/to osteosclerosis



Dialysis for renal diseases

- Dialysis dementia (Aluminium toxicity) develops many years after dialysis disequilibrium .
- Clff which can improve after dialysis
 - High K^+ refractory to medical t/t
 - Metabolic acidosis
 - Fluid overload/ pulmonary edema
 - Uremic manifestations
 - Encephalopathy → Esterexis, seizures, myoclonus
 - Pericarditis → Pericardial rub
 - Peripheral neuropathy → Restless leg syndrome

○ *CI/f which do NOT improve after dialysis*

- Splenomegaly
- Low HDL
- Growth retardation in children
 - Infertility
 - Sleep disturbances
 - Myopathy
 - Anemia
 - Osteodystrophy

○ *CI/f which progress/develop after dialysis*

- Thrombocytopenia

Cryoglobulinemia

○ M/c infection a/w essential mixed cryoglobulinemia (EMC) is **hepatitis C**.

○ 3 types:

Type I : Single, monoclonal Ab (Ig M type)

Type II : Mixed, monoclonal Ab (Ig M + Fc portion of IgG type)

Type III : Mixed, polyclonal Ab (Ig M + Fc portion of IgG type)

○ *CI/f:*

- Triad of **palpable purpura + arthralgia + myalgia** (*Meltzer's triad*) is seen in polyclonal cryoglobulinemia.
- Hyperviscosity, livido reticularis, gangrene
- Type II & III produce extravascular manifestation
 - Renal → Immune complex GN (**Low C3**)
 - Joint → Polyarthritides
 - Lungs → Bronchiectasis.

Polycystic ds of kidney (PKD)

○ Both kidneys are grossly enlarged with multiple cyst. A/w cylindrical dilatation of tubules.

○ Pathology: Ciliopathy.

○ Inheritance : **AD** in **Adult** PKD & **AR** in children [Remember **AD** in **AD**ult].

Defective gene is located on chromosome **16 & 4** but in **AR** PKD it is on chr.6

○ *Renal manifestations :*

Renal symptoms are most common. Pt presents in 3rd/4th decade with **b/L chronic flank pain**. Acute pain suggests infection, hemorrhage, or stone formation. b/L renal mass, hematuria, nocturia, CRF, HTN can be seen. Presence of **HTN** is m/c sign (more common in adults than children).

○ *Extrarenal manifestations :*

- Hepatic cysts are m/c extrarenal findings. found in 50-70% of cases and are usually asymptomatic (Normal LFT).

Cysts in **liver** (m/c) > spleen, pancreas, ovary.

- May be a/w Potter facies & oligohydramnios
- Colonic diverticula (**m/c GI anomaly**),
- Berry's aneurysm (5-10% **m/c CVS anomaly**),
- MVP (**m/c CVS finding**), AR, TR

○ Prognosis is generally poor

○ '**Spider leg appearance**' on IVU.

Renal Vein Thrombosis (RVT)

○ **1° :**

Dehydration is the m/c cause of RVT in newborns. Nephrotic syndrome is the m/c cause of RVT in adults. NS may be d/to membranous glomerulopathy (MGP has strongest association with RVT), MPGN, amyloidosis, lupus nephritis.

○ **2° :**

Trauma, extrinsic compression (LN, tumour, aortic aneurysm), Invasion by RCC, pregnancy, OCPs use.

○ Rim sign is seen.

- *Nephrocalcinosis is a feature of medullary sponge kidney.*
- *Membranous glomerulopathy has strongest association with RVT (renal vein thrombosis).*
- *Reflux nephropathy leads to nephron loss / FSGS.*
- *Hepatitis C is a/w 2° MPGN, cryoglobulinemic glomerulopathy & MGN.*
- *Leprosy is a/w MGN.*
- *Neonatal kidney achieve concentrating ability of adult kidney by 12 months.*

Analgesic Nephropathy

○ M/c cause : Analgesic abuse

○ Finding: Renal papillary necrosis

○ Other causes of renal papillary necrosis :

DM, Sickle cell d/s,

Familial hypocalcemic hypercalciuria

○ **AD**

Presents as asymptomatic hypercalciuria

○ **FHH and Jansens** are variant of primary hyperparathyroidism c/by ↑ PTH secretion and biological activity of PTH receptor in target tissue

○ Primary defect is abnormal secretion of Ca^{++} by renal tubules thereby resulting in ↑ PTH secretion.

- D/d: with primary hyperparathyroidism in which <99% renal calcicum reabsorption while in FHH > 99%
Average age for primary hyper parathyroidism <10 years while FHH first decade.
- Urine analysis reveals isomorphic RBCs and absence of casts.

TUBERCULOSIS (TB)

- There are 3 clinicopathological consequences of progressive pulmonary tuberculosis :
 - Cavitory fibrocaseous tuberculosis
 - Miliary TB
 - Tuberculous bronchopneumonia
- TB may complicate & progress to --- Serous pleural effusion, empyema, massive obliterative pleuritis.
- **Primary complex =**
Subpleural parenchymal focus + draining LN + Lymphatics (Ghon focus)
Ghon's complex
- The m/c symptom of pulmonary TB is persistent cough for 3 weeks or more usually a/w expectoration.

- Ziehl-Nelson's method is m/c used or traditional method.
- AR (auramine-rhodamine) staining, is a screening method, more sensitive than ZN staining, used to examine several smears at a time.
- Sputum microscopy (ZN staining of sputum smear and examination under direct microscopy) is the gold standard & is the method of choice as a case finding tool. It is most reliable single method in diagnosis and control of TB.
Microscopic demonstration of acid-fast bacilli provides only presumptive evidence of TB infection.
- Sputum culture is used for smear -ve cases and to monitor response to drug treatment, also used for MDR TB.
- Quantiferon Gold (interferon γ soluble Ag detection) test is useful for detection of latent infection.
- MMR (mass miniature radiography) is not used now.

Interpretation of Sputum smear in RNTCP

No. of AFB	Result	Grading	No. of fields examined
0 (AFB not seen)	-ve	Negative	100
1-9 per 100	+ve	Scanty	100
10-99 per 100	+ve	1+	100
1-10 per OIF	+ve	2+	50
>10 per OIF	+ve	3+	20

- Patient suspected to have pulmonary TB should have 2 sputum smears examined collected on 2 consecutive days. Patient with only 1 positive result should undergo CXR examination
- 10% of TB suspects are expected to have SSP pulmonary TB

Acc/to RNTCP Categories of t/t or DOTS short course chemotherapy regimes

T/t category	Type of patient	Regimen
Cat I	New sputum smear positive (SSP) Seriously ill New sputum smear negative (SSN) Seriously ill New EPTB	$2H_3R_3Z_3E_3$ + $4H_3R_3$
Cat II	SSP relapse, SSP failure, SSP retreatment after default	$2H_3R_3Z_3E_3S_3$ + $1H_3R_3Z_3E_3$ + $5H_3R_3E_3$
Cat III	Not- seriously ill new SSN Not-seriously ill New EPTB	$2H_3R_3Z_3$ + $4H_3R_3$

- In revised RNTCP program (2010) only 2 categories of pediatric tuberculosis are there. Cat I & Cat II

• Seriously ill TB

Meningitis, Pericarditis, peritonitis, B/I or extensive pleural effusion, spinal TB with neurological involvement, intestinal/ genitourinary TB, Coinfection with HIV, all form of pediatric EPTB (other than LN TB and U/L pleural effusion)

Forms of smear negative PTB which are classified as seriously ill are :

Milliary TB, cavitory d/s, extensive parenchymal infiltration, TB with HIV coinfection, all forms of pediatric SSN

PTB except primary complex

• Not Seriously ill TB

LN TB, U/L pleural effusion, peripheral joints involvement

HIV / AIDS

- HIV belongs to family retroviridae (subgroup lentiviridae). HIV is a retrovirus which forms its DNA from RNA with the help of enzyme reverse transcriptase (RNA dependent DNA

polymerase). Genome is composed of *two identical single standard +ve sense RNA* copies with reverse transcriptase enzyme.

- In India **m/c** strain of HIV is HIV-1 and subtype is C while HIV-1 subtype A is most prevalent worldwide.
- Both HIV-1 & HIV-2 are zoonotic infections. Pan troglodytes spp of chimpanzees has been established as the natural reservoir of HIV-1
- HIV enters via CD4. HIV-1 utilizes two major co-receptors along with CD4 to bind to, fuse with, and enter target cells; these co-receptors are CCR5 and CXCR4.

CCR5

Strains of HIV that utilise CCR5 as coreceptor are referred to as **R5 viruses**. More efficient in infecting monocytes/macrophages and microglial cells of the brain. Predominates during early stage of d/s. CC chemokines RANTES (CCL5), MIP1a (CCL3), MIP1b (CCL4), which are natural ligands for CCR5, block entry of R5 viruses.

CXCR4

Strains of HIV that utilise CXCR4 are referred to as **X4 viruses**.

R5X4 viruses

Many virus strains are dual tropic and referred as R5X4 viruses

- The mechanism whereby the CC chemokines RANTES (CCL5), MIP-1a (CCL3), and MIP-1b (CCL4) inhibit infection of R5 strains of HIV or SDF-1 blocks X4 strains of HIV involve blocking of the binding of the virus to its co-receptors, the CC chemokine receptor CCR5 and the CXCR4-chemokine receptor CXCR4, respectively.
- In HIV positive individuals/AIDS
 - **M/c** malignancy --- Kaposi Sarcoma (70%)
 - **M/c** Space occupying lesion --- Toxoplasmosis > NHL (2nd **m/c**)
 - **M/c** ICSOL in AIDS patient --- Lymphoma
 - **M/c** cause of seizures --- HIV encephalopathy > Toxoplasmosis
 - **M/c** fungal infection --- Cryptococcus neoformans
 - **M/c** lymphoma (NHL) --- B-cell immunoblastic lymphoma (CNS lymphoma)
 - **M/c** cause of blindness --- CMV retinitis
 - **M/c** eye lesion --- Cotton wool spots, HIV keratitis.
 - **M/c** CNS manifestation --- HIV encephalopathy (60%)
 - **Mc** reservoir cell in CNS --- Microglial cell.

- **M/c** opportunistic infection --- Pneumocystis carinii (Tuberculosis in India)
- **M/c** CXR finding in TB with HIV --- Miliary shadows
- **M/c** electrolyte abnormality --- Hyponatremia, SIADH
- **M/c** cause of diarrhoea --- Cryptosporidium
- **M/c** genital lesion --- Herpes

- CVS c/c of HIV : DCM with CHF, pericardial effusion, tamponade, NBTE, etc.

Absolute CD₄ counts & opportunistic infections

<500/ μ l	<200/ μ l	<50/ μ l
TB	Pneumocystis carinii	Disseminated
Herpes	Toxoplasma	MAC
Vaginal candidiasis	Cryptococcus	CMV retinitis
Hairy leukoplakia	Coccidiomycosis	Histoplasma
Kaposi's sarcoma	Cryptosporidium	CNS Lymphoma

- Full blown AIDS develop when CD4 count falls < 200.

Tests

- **ELISA test** is an antibody test which is most widely used. It **first screening test** (highly sensitive but less specific). Direct solid phase anti-globulin ELISA is **m/c** employed method.
- **Western blot test** is **confirmatory** test and is highly specific (specific enough to record false +ves). This test is based on detection of specific antibodies to viral core protein (p 24) & envelop glycoprotein (gp 41)]

Antigen	Represent	Coded by
P 24	Core protein (shell)	gag gene
P 31	Reverse transcriptase	pol gene
gp 160 {gp 41, gp 120}	Surface antigen (envelope glycoproteins)	env gene

- **Other tests, used if WB is indeterminate:**

1. p 24 antigen capture assay
2. HIV-1 RNA assay
HIV RNA by bDNA, NASBA or PCR
3. HIV- DNA PCR
4. Ora quick Rapid HIV-1 antibody test.
(~99% sensitive & specific)

As the most sensitive & specific test PCR has become

the gold standard for D/g in all stages of HIV-infection including window period. PCR measures the viral load in peripheral blood as number of viral copies/ml of blood.

- *Window period* : It may takes 4-8 wks for antibodies to appear in blood after infection. This seronegative but highly infective stage when standard antibody tests are -ve is WP. Infection can be detected by **P 24 antigen assay** or PCR.

○ *Early diagnosis of HIV in infancy*

3 viral detection assays are useful : DNA or RNA PCR, HIV culture & p24 antigen assay.

HIV-DNA-PCR is the preferred & earliest diagnostic method for HIV-1 subtype B (40% of infected newborns are +ve in 1st 2 days of life and >90% by 2 wks).

RT PCR is more sensitive and best for earliest d/g in infants >18 months and to identify non B subtype.

- D/g of HIV in <2 months old infant is done by ELISA.
- HIV associated nephropathy is severe form of FSGS
- Characteristically severe collapsing glomerulopathy, visceral epithelial cell swelling occur.
- Presents with nephrotic range proteinuria and hypoalbuminuria without HTN, edema, hyperlipidemia.
- PCP (Pneumocystis Carinii Pneumonia) is diagnosed by BAL & treated by co-trimoxazole (TMP-SMX)
- Reverse transcriptase sequence in HIV is RNA--DNA--RNA
- Quantiplex bDNA or branched DNA test is recent nucleic acid based test.

- *ARC (AIDS Related Complex)* : A term used in early years of AIDS epidemic to describe people with HIV infection + mild symptoms like generalised lymphadenopathy. There is ↑ or hyperactive B-cell humoral responses (cf ↓ antibody response in AIDS) & follicular/mixed hyperplasia of LN.

HIV & Tuberculosis

- T/t of HIV in a patient of TB : Zidovudine+ lamivudine+ Abacavir. Give rifabutin in place of rifampicin.

○ *Comorbidity/ Risks*

↑ed	↓ed	Same
1. Reactivation	MT positivity	Chances of MDR-TB
2. D/s progression	Cavity	Response to short course chemo
3. Extrapulmonary	Upper zone involvement	
4. Miliary		
5. LN -pathy, skin reaction to ATT		

indications for changing ART in patient with HIV infection

- < 1-10g ↓ in plasma HIV-RNA titre after 4 wks of ART
- > 3 fold ↑ from nadir (significant ↑) not attributed to infection, vaccination/method.
- Persistently declining CD₄+ T-cell no.
- Clinical deterioration
- Side effects (toxicity)
- CDC case definition of AIDS include all HIV infected individuals with CD₄+ T cells counts < 200
- Immune reconstitution inflammatory syndrome (IRIS) is seen m/c in patients starting therapy with a CD₄+ T cells counts < 50/ μL who experience a precipitous drop in viral load following initiation of HAART

Immunizations generally recommended for prevention of opportunistic infections in pt with HIV/AIDS

HBV, HAV, Pneumococcal vaccine, HPV vaccine

Newer drugs in T/A

- **Maraviroc** : CCR5 inhibitor
- **Raltegravir** : Integration inhibitor
- **Enfuvirtide** : p 24 entry inhibitor

- Primary prophylaxis against these infections would be appropriate in a pt with HIV infection & a CD₄ count below 100/mm³ — CMV, Cryptococcal meningitis, PCP
- In an asymptomatic pt with HIV infection a definite indication for starting anti-retroviral therapy (ART) is CD₄+ count < 350 cells/ μL.
- In an asymptomatic pt with HIV infection and normal CD₄+ count a potential indication for starting anti-retroviral therapy (ART) would be a viral load above 100,000 copies/ml
- A single positive virological assay (detection of HIV by PCR, culture or p24 antigen) suggests HIV infection and should be confirmed by repeat test.
- In any child >18 month demonstration of IgG antibodies to HIV by ELISA & western blot establishes the diagnosis of HIV infection.

DIABETES MELLITUS (DM)

Type-I Vs. Type-II Diabetes Mellitus

Features	DM-I (IDDM / JOD)	DM-II (NIDDM, MODY)
Occurrence	10-20%	80-90%
Concordance in twins	50%	95%
Onset	Early (juvenile onset)	Late onset (>40 year) (maturity onset)
Normal weight	Yes	No (Obese)
HLA association	Yes (HLA DR ₃ , DR ₄)	No
Islet cell antibodies, insulinitis (Autoimmune phenomena)	Yes	No
Insulin sensitivity (response)	Yes	No (insulin resistance +nt) [But respond to SU]
Frequent complication	DKA	Non-ketotic hyperosmolar coma
Glucagon	High, suppressible	High, Not suppressible
Blood insulin	↓	Normal or ↑
Pathophysio	Severe lack of insulin caused by reduction in B-cell mass	Insufficient insulin secretion relative to glucose load.

→ Remember that most of the points in type-II DM are— no, non and not

→ Type-I DM, malnutrition related DM & pregnancy related DM is associated with HLA.

Criteria for diagnosis of DM

- WHO 2011 : An HbA1c of 48 mmol/mol (6.5%) is recommended as the cut point for diagnosing diabetes.
- Older criteria:
 - Symptoms of diabetes + RBS > 200 mg% (>11.1mmol/L)
 - Fasting plasma sugar > 126 mg% (>7mmol/L)
 - 2 hour plasma glucose > 200 mg% (>11.1mmol/L) during an oral GTT
- Ketosis is absent because of subnormal β -cell function & absence of hyperglucagonemia.
- GLYCEMIC INDEX :
 - White bread : 100
 - White rice : 89
 - Milk , full cream : 41

Malnutrition related DM (MRDM)

- M/c type of diabetes in India a/w PEM (Kwashiorkor). In tropical countries onset < 30 yr
- Hallmark is non dependence on exogenous insulin to prevent ketosis.
- Ketosis is absent because of subnormal β -cell function & absence of hyperglucagonemia
- A/w environmental toxin cassava (tapioca), fibrocalceous pancreatic diabetes
- Protein deficiency is responsible for CBH intolerance in Kwashiorkor & also fasting normo-or hypoglycemia is present in Kwashiorkor.

Honeymoon phase

When insulin requirement is decreased to $\leq 50\%$. This is f/b overt diabetes. D/to residual β -cell function

Somogyi phenomena

- Refers to wide swings in insulin levels (*hypoglycemia begetting hyperglycemia*). Rebound nocturnal hypoglycemia with sweating, headache is followed by morning hyperglycemia d/to release of counter regulatory hormones. Usually seen in patient given excess insulin
- If suspected, insulin **dose** adjustment is required (dose should be ↓ ed).

Dawn phenomena

- Is early morning hyperglycemia (5-9 a.m.) without a preceding nocturnal hypoglycemia d/to exhaustion of biologically available insulin. Both midnight and early morning RBS is high.
- There is overnight GH secretion (predawn surge of GH in IDDM) and increased insulin clearance and, hence the **night dose of insulin has to be increased**

Complications in DM

- Life threatening infections a/w DM are ---Rhino cerebral mucormycosis, emphysematous pyelonephritis & appendicitis
- Other less severe infections a/w DM are ---Malignant otitis externa
- Silent MI may occurs

Microvascular complications in DM are

- Diabetic nephropathy
- Diabetic retinopathy (NPDR/PDR, macular edema)
- Diabetic neuropathy (Sensory, autonomic)

Macrovascular complications in DM are

- CAD (Coronary artery d/s),
- CVD (Cerebrovascular d/s)
- PAD (Peripheral vascular d/s)

Skin manifestations of DM :

- Necrobiosis lipodica diabetica : Front of leg
- Acanthosis nigricans: Nape area

Diabetic nephropathy

- Microalbuminuria is the most sensitive for early diagnosis of diabetic nephropathy.
- Urine microalbumin to creatinine ratio (MAU : U_{Cr}) is important for early diagnosis
- M/c renal lesion in DM is diffuse glomerulosclerosis but nodular glomerulosclerosis with **Kimmelsteil Wilson wire** lesions are most pathognomonic
- Renal amyloidosis may develop.
- Glycosylated Hb reflects the mean blood glucose level of previous 3 months.

Diabetic neuropathy

- Hypoglycemia unawareness may occur.
- Glove and stockings type of peripheral neuropathy.
- ANS dysfunction.
- M/c form of diabetic neuropathy is distal symmetric sensorimotor polyneuropathy (DSPN).
- Mononeuropathy is less common. Involvement of 3rd CN (oculomotor) nerve is m/c & is heralded by diplopia. Ptosis + diplopia + ophthalmoplegia with pupillary sparing.

Factors Affecting Insulin Requirement

Stimulator	Inhibitor
Amino acids	Epin, NE
Drugs (Theophylline, SU, β -agonist)	Drugs (Diazoxide, thiazide, phenytoin, propranolol)
Ach, cAMP	Somatostatin
Intestinal hormones (GIP, gastrin, secretin, CCK)	K^+ depletion

- Insulin sensitivity is \uparrow ed with progress of renal insufficiency. As a rule, insulin requirement declines in cases with renal failure, exercise.
- Insulin requirement is increased in high calorie intake, hyperadrenalism (d/to high EpiN, NE, glucocorticoid)

- In animals with experimental diabetes, adrenalectomy markedly ameliorates the diabetes.
- If a patient with hyperglycemia is given insulin, it results in --- Hypokalemia

Newer Drugs

- DPA IV inhibitor : *Vidagliptin, Sidalglipitin*
- Glucagon like peptides (GLP) : *Exentide, Liraglutide*
- Amylin analogue : *Premalinitide*.
- Therapy which can results in β cell preservation : Incretins.

CONNECTIVE TISSUE DISORDERS (CTD)

SLE

- SLE like syndrome (**drug induced lupus**) is seen with – Hydralazine, procainamide, INH, Penicillamine, methyl dopa, carbamazepine
[Mnemonic: PIH Pt consumes methyl dopa]
- Cardiac/f are – **Pericarditis (m/c)**, Libman sacks (verrucous) endocarditis, heart block, valvular incompetence.
- Characteristic renal lesions are – wire loop lesions, membranous GN & focal GN
- Typical skin lesions are – Erythematous "**Malar butterfly rash**"
- Most specific antibody for SLE is anti-ds DNA & anti-Sm. For drug induced lupus it is anti-histone.
- Bad prognostic factors are – hypocomplementemia, anti-ds DNA & persistent proteinuria $> 3\text{gm/d}$
- Increased excretion of prostaglandin L is seen in lupus nephritis
- M/c eye lesion is – Sicca syndrome
- SLE is a cause of habitual abortions, coomb's positive hemolytic anemia (AIHA), non-erosive arthritis, myalgia and arthralgia, polyserositis.
- Indications of steroid are – polyserositis, neuropsychiatric manifestations, nephrotic syndrome (MGN), myo/pericarditis, thrombocytopenia .

- Imp. findings NOT seen in SLE are --- Erosions in joints, joint deformities, sterility
- Chloasma is char/by non erythematous rash over face which is seen post pregnancy
- Imp. findings NOT seen in polymyositis are --- Ocular/ facial m/s involvement, rash, F/H, m/s dystrophy

In SLE

- Most sensitive antibody is --- ANA (+ve in 80% of cases)
- Specific antibody is --- Anti - ds DNA (Rim or peripheral staining pattern on immunofluorescence studies)
- Most specific antibody is --- Anti - Sm (Speckled pattern on immunofluorescence studies). Marker of CNS lupus.
- Most specific / characteristic antibody for drug induced lupus --- Anti - Histone
- **Anti - Ro (SS-A)** is positive in Sjogren/ sicca syndrome, neonatal lupus (a/w congenital heart blocks) and ANA -ve lupus

→ ANA in drug induced lupus are m/c d/to : Procainamide in 75% > Hydralazine 30%

→ To detect ANA on immunofluorescence rat liver sections are used.

→ Anti ds DNA is specific & diagnostic test for SLE.

→ Anti topoisomerase- I is marker for systemic sclerosis.

- In scleroderma
 - In Diffuse systemic : Anti - topoisomerase Ab sclerosis (S Sc)
 - In CREST syndrome : Anti-centromere ab (limited S Sc)
- Localized scleroderma : Anti-centromere ab
- In MCTD : Anti - U₁ RNP Ab
(Anti U₁ RNP is a Antinucleolar antibody)

POLYMYOSITIS / DERMATOMYOSITIS

- Autoimmune in origin
- Skeletal m/s is damaged by non-suppurative inflammatory process dominated by lymphocytic infiltration.
- **Cl/f :**
 - Polymyositis spares skin, while dermatomyositis is a/w characteristic skin rash (**Heliotrope, Gottron's rash**)
 - In polymyositis there is symmetrical weakness of proximal muscles (of pelvic, shoulder girdle) but **ocular/ extraocular muscles are never involved**.
 - Incidence of neoplasia is higher in pt. over 40 yrs. age.

M/c associated malignancies are lung, breast, ovary, GIT and lymphoproliferative d/s.

- Cutaneous manifestations of dermatomyositis are --- Severe itchy lesions, **heliotrope skin rash, Gottron's papules**, nail fold telangiectasias, poikiloderma, shawl sign, **mechanics hands**, calcinosis cutis.

Lab/f:

- Dermatomyositis typical skin rash, m/s weakness, EMG changes, ↑ serum CK (*no need of m/s biopsy*)
- Polymyositis typical clinical features, EMG, serum CK ↑ and diagnostic m/s biopsy.
- Specific antibody in myositis : Anti Jo-1

T/t:

- Glucocorticoids
- If no response to GC's than cytotoxic therapy c/b given.

→ Imp. findings NOT seen in polymyositis are --- Ocular/ facial m/s involvement, rash, F/H, m/s dystrophy

SJÖGREN'S SYNDROME

- It is chronic, slowly progressive, autoimmune disease characterized by lymphocytes infiltration of exocrine glands resulting in **xerostomia (dry mouth) + dry eyes** (keratoconjunctivitis sicca or **Sicca syndrome**)
- **Cl/f:**
 - Middle aged women affected
 - Xerostomia + kerato- conjunctivitis sicca + parotid enlargement
 - Arthralgia/arthritis, Raynaud's phenomenon
 - Lung involvement
 - Vasculitis
 - Lymphadenopathy, Lymphoma and Waldenström's macroglobulinemia
- A/w other autoimmune d/s most commonly RA, other like SLE, scleroderma, PBC, Vasculitis etc.
- *Drugs causing dry eye / keratoconjunctivitis sicca:* Sulfonamides (sulfadiazine, sulfasalazine), aspirin
- **T/t:** Usually symptomatic. Glucocorticoids for extraglandular manifestation.
Etanercept, Infliximab, TNF inhibitors.

SCLERODERMA (Systemic Sclerosis)

- Multisystem d/s d/to fibrosis of skin, blood vessels, and visceral organs including GIT, lungs, heart, kidneys.
- **Cl/f:**
 - Young females in 3rd-5th decade affected.
 - M/c symptom : Raynaud's phenomena (sausage digits c/b seen)
 - Skin → Calcinosis, ulcers, fibrosis, thickening.
 - GIT → Dysphagia, muscularis atrophy, **pseudo-obstruc^a**
 - Lung → ILD/ pulmonary fibrosis (*leading cause of death*)

- Kidney → Renal failure. Scleroderma renal crisis is precipitated by: Sulfonamides, Hydralazine, Procarbazine, INH.
- Skeletal → Symmetric polyarthritis, fibrosis (tightening of fingers), **resorption of bone**
- CVS → Pericarditis, heart block/ failure, arrhythmias

○ Lab/f :

- **Anti-topoisomerase I** antibody in ---- Diffuse SSc.
- **Anticentromere** antibody in --- limited SSc (Scleroderma) a/w good prognosis
- ESR ↑
- Anemia, hypergammaglobulinemia, ↑ IgG.

○ T/t :

- No specific T/t
- t/t of involved organ is done with penicillamine, glucocorticoids, CCB's, antacids.

CREST Syndrome (Limited Systemic Sclerosis)

- CREST stands for Calcinosis, Raynaud's phenomena, Esophageal hypomotility, Sclerodactyly, Telangiectasias
- Anticentromere antibody is seen which indicates good prognosis

Indication of Glucocorticoids in SLE & RA

In SLE	In RA
Nephritis	Pericarditis
Hemolytic anemia	Perforating eye lesion
Pericarditis/Myocarditis {But not endocarditis}	Active and progressive disease.
Alveolar hemorrhage	
CNS involvement, convulsions	
TTP	

Mixed Connective Tissue Disease (MCTD)

- It include combination of symptoms of SLE, SSc, polymyositis.
- **CI/f** : Presenting feature is Raynaud's phenomenon, puffy hands, arthralgia, myalgia and fatigue.

Pulmonary involvement occurs in 85% of cases. Membranous GN is common.

- **Lab/f** : Anemia, +ve direct Coomb's test, leucopenia, thrombocytopenia, hypergammaglobulinemia.
- Antibodies to U₁RNP.

MISC. TOPICS

Wilson's disease

- Also k/as *hepatolenticular degeneration*
- Autosomal recessive metabolic disorder d/to accumulation of copper in hepatocytes
- Mutation in gene on **chromosome 13** (ATP B7)
- Basic defect
 - Reduced biliary excretion of copper. Copper saturates liver, spills in plasma and spreads to other organs.
 - Deficiency of ceruloplasmin (a copper binding protein in plasma)

○ Patho

- Copper content of substantia nigra is high
- Severe degeneration of lentiform nucleus

○ CI/f

- Younger patients present with liver disease while older patients present with neurological disease
- Hepatitis (all forms of hepatitis may be seen - acute, fulminant, chronic active, cirrhosis)
- Coomb's negative hemolytic anemia, splenomegaly

○ CI/f

D/to Cu deposition in

1. Basal ganglia : '*Bats wing*' tremors, cerebellar ataxia, **chorea**, spasticity/ rigidity, dysphagia, dysarthria. Asterexis/liver flap is d/to copper deposition in caudate nucleus.

[*Sensory changes are never seen*]

2. Descemet membrane of cornea :

Kayser - Fleisher ring (greenish brown ring seen at the periphery of cornea in deep layers of descemet's membrane), sunflower cataract

[*No effect on vision d/to KF rings*]

3. Genitalia :

- Amenorrhoea
- Recurrent abortions

4. Kidney :

- Microscopic hematuria
- Nephrocalcinosis → renal calculi

5. Psychiatric :

- Loss of emotional control, depression, ↓ sexual drive

● Supportive lab/f

- ↓ in serum copper & in ceruloplasmin copper
- ↑ in free copper content ($> 200 \mu\text{g}/24 \text{ hr}$)
- ↑ **urinary copper excretion** ($> 100 \mu\text{g}/24 \text{ hr}$)
- ↑ Copper deposition in liver tissues
- ↓ ceruloplasmin levels ($< 18 \text{ mg}\%$)

● Liver biopsy is definitive and gold standard Ix.

● T/t

1. For initial hepatic manifestations
 - without decompensation : Zinc
 - with decompensation: Cu - chelators (Trientine & Penicillamine)
1. For initial neuro-psychiatric manifestations
 - Tetrathiomolybdate

Cystic fibrosis (*Mucoviscidosis*)

- Autosomal recessive disorder d/to mutation in the CFTR gene located on **chromosome 7**
- Char/by epithelial dysfunction, sinusitis, ↑ed sweat chloride, azoospermia. Altered pH of surface secretions.
- H. influenzae, and S. aureus are m/c organism recovered from lung secretions
- Meconium ileus is typical in newborn . Distal intestinal (colonic) obstruction is seen.
- D/g : **Immunoreactive trypsinogen** and **CFTR** gene are the markers of d/s activity. Nasal pn-d estimation is als o useful. IRT is a screening test in newborn for CF. Sweat chloride test is another useful test.
- CXR reveals hyperinflation & small airway obstruction in early stage and bronchiectasis in later stage.
- T/t : Pancreatic enzyme replacement, replacement of fat soluble vitamins particularly **vitamin E and K** is useful.

Hemochromatosis

- Disorder of excessive iron storage c/by deposition of excessive iron in parenchymal cells
- **Hereditary H~** is an AR condition which is genetically heterogenous and is a/w mutations in HFE gene located on chromosome 6p and is HLA-A linked. Common in males. A/w incomplete penetrance. A/w cardiomyopathy and DM, hepatic cirrhosis, SCA, HS, sideroblastic anemia, congenital dyserythropoietic anaemia.
- 2° hemochromatosis results from hemoglobinopathies like β -thalassemia,
- Excess iron is deposited in liver, heart & pancreas
- Liver is the first & m/c organ to be affected (95%).

● C/f

Hyperpigmentation, diabetes mellitus (**bronze diabetes**), arthritis/arthropathy, gynecomastia, testicular failure, hypogonadism, cardiac failure (cause of death)

● Lab/f

- ↑ in % transferrin saturation ($> 45\%$) is the earliest phenotypic abnormality in hereditary h~.
- ↑ in serum iron , s. ferritin.
- ↓ in UIBC (unbound or unsaturated iron binding capacity). $\text{UIBC} = \text{TIBC} - \text{Serum iron}$
- liver biopsy is diagnostic

- T/t - Desferoxamine is TOC (but not in hereditary h~), phlebotomy

Idiopathic Pulmonary Hemosiderosis

- Condition affecting lungs
- Also k/as essential brown induration of lungs or Ceelen-Gellerstedt syndrome
- Triad of hemoptysis + IDA (anemia) + diffuse pulmonary infiltrates
- There is sudden ↓ in hct level with the onset of active respiratory d/s

SARCOIDOSIS

- Characterized by non caseating epithelioid granuloma on pathology & radiologically by:
B/L hilar lymphadenopathy with egg shell calcification (hallmark), miliary shadow, pleural involvement .
Garland triad : consist of enlarged Rt paratracheal LN + Rt. hilar LN + Lt hilar LN (1-2-3 sign).
- Lab/f
 - Positive Kveim's skin test,
 - Schaumann's bodies, Asteroid bodies, Conchoid bodies within giant cells
 - RA factor may be +ve ,
 - Angiotensin converting enz. (ACE) level in blood is raised which indicates severity of ds
 - T_H cells & lymphocytes are increased locally (at the site of d/s $\text{CD4} : \text{CD8}$ ratio is very high may be upto 10:1 in BAL) but no. of T_H cells in the blood are normal
- In childhood S~ is a/w **B/L parotid enlargement** (parotitis), a high incidence of spontaneous remission
- Clinically S~ causes addison's disease, DI, **hypercalcemia**, **uveitis**, (adrenal gland involvement is rare)
 - Respiratory symptoms are m/c presentation
 - Lung involvement in form of ILDs, pleural effusion &

rarely cavitation

- Skin involvement in form of **skin nodules** (erythema nodosum) & lupus pernio
- M/c CN involved is **7th (facial n)** with u/L facial palsy. Other CN involved are 3,6,9.
- Biopsy confirms diagnosis.
- Tuberculin test is negative.
- DOC is glucocorticoid.

ASBESTOSIS

- Asbestos is of 2 types — serpentine (chrysolite) and amphibolite (crocidolite, amosite etc.).
90% of asbestos is of serpentine (chrysolite) variety.
- Chrysolite & amosite are safer variety of asbestos
Asbestosis is most commonly a/w crocidolite fibres.
- Asbestos dust may be deposited in the alveoli & affects bases of lungs. Fibres are insoluble .
- Lung fibrosis is diffuse & **basal** (in contrast to silicosis in which fibrosis is nodular & in upper zone).

Lung changes	Silicosis	Asbestosis
Fibrosis	Nodular	Diffuse
Involves	UZ	LZ/ basal

- A *ferruginous body* is a macrophage derived histological finding in **ILD/ asbestosis** that is a result inorganic dust inhalation and is seen on H& E stain.
- Asbestosis leads to:
 1. Pleural plaques: Develops within 1-2 yr. Involves lower/ diaphragmatic pleura. Indicates exposure but no lung damage.
 2. Pulmonary & pleural fibrosis
 3. Pleural effusion : Hemorrhagic, asymmetrical, eosinophilia+
 4. Asbestosis takes 10-15 yrs to develop. Lower lobe interstitial pattern on CXR
 5. Retroperitoneal fibrosis
 6. Cancers
 - a) Ca bronchus/lung : 15-20 yrs, a/w smoking. Lung cancer is m/c cancer in asbestos exposed persons.
 - b) Cancers of GIT
 - c) *Mesothelioma*: No relation with smoking, ascites+, effusion+. It is a very rare cancer of pleura/ peritoneum, **Strong a/w** asbestos exposure (esp. of crocidolite amphibolite variety)
- CXR shows a ground glass appearance in lower 2/3rd of lungs.

FAT EMBOLISM

- Fat embolism of lungs typically appears 12 to 72 hours (lucid interval) after long bone # especially of the femur or tibia.
- Also observed a/w acute pancreatitis, parenteral nutrition of lipids, liposuction, cardiopulmonary bypass etc.
- *Bergman's triad* of **arterial hypoxemia + mental confusion (delirium) + petechiae** especially over ant. neck, shoulders & chest.
- Arterial hypoxemia is always present and may progress to ARDS
- In cerebral F~ retinal vessels involved. **Cerebral purpura** in white matter of brain may occur.
- Lipiduria (**fat globules in urine**)
- T/t - O₂ and high dose glucocorticoids are used.

AIR EMBOLISM

- Seen after intracranial surgeries performed in sitting position (sitting craniotomies), CVC insertion/removal, intra op in cases which are performed in reverse trendelenberg positions.
- Signs---unexplained hypotension, tachycardia, sudden decrease in EtCO₂.
- Gold standard test is --- Angio
- Most sensitive & IOC is --- TEE (Trans esophageal echocardiography).
- HBO (Hyperbaric oxygen therapy) is TOC for arterial AE.
- Mill-wheel murmur is a late sign

PSEUDOTUMOUR CEREBRI

- Also k/as **Benign** idiopathic intracranial hypertension
- D/to raised ICT probably resulting from impaired CSF absorption by arachnoid villi
- C/I/F morning headache that is worsened by coughing/ straining, b/L papilloedema
- Most patients are young, female, obese
- Drugs causing P~: **Glucocorticoids, Vitamin A toxicity, tetracycline, OCPs, Nalidixic acid, nitrofurantoin**
- Characterized by ↑ICP with a >20mm Hg, normal sensorium, normal CSF cell counts and proteins and normal ventricular size.
- T/t - usually self - limiting, monitoring of visual acuity, acetazolamide, repeated LP.
In contrast malignant hypertension is characterized by b/L papilloedema, macular star, silver wiring of arterioles (highly exaggerated light reflex).

- ↑ CSF proteins is seen in — infections, ICH, GBS, MS (multiple sclerosis), malignancies.
- ↓ CSF proteins is seen in — Repeated LP, pseudotumor cerebri, etc. (but not in hypothyroidism)

Normal Pressure hydrocephalus

- Characterized by triad of
 - Dementia (memory loss)
 - Apraxic gait (gait disturbances)
 - Urinary incontinence
 K/as Adam's or Hakim's triad.
- On CT - lateral ventricles are enlarged but minimal or no cortical atrophy (communicating hydrocephalus with patent aqueduct)
- On LP - Opening pressure is in high normal range. CSF biochemistry is normal.

PORPHYRIA

- M/c type --- PCT (d/to def. of *uro-P-decarboxylase*, max^m photosensitivity)
- All porphyrias are AD disorder but Congenital erythropoietic P^r is AR
- Psychiatric manifestation are common in --- AIP
- Photosensitivity is seen in all types but NOT seen in --- AIP
- Erythropoietic protoporphyria is d/to def. of *ferrochelataase*
- Congenital Erythropoietic protoporphyria is d/to def. of *uroporphyrinogen III synthase*
- Increased urobilinogen in urine is seen in --- AIP, Variegate P~, Hereditary P~.

SOME POINTS OF SPECIAL MENTION

- **Subendocardial hemorrhages** are flame shaped hemorrhages seen in LV, on left side of IVS on the opposing papillary m/s and adjacent columnae carnae. Hemorrhages are flame shaped, confluent and tend to occur in continuous sheets.
- **Iloprost**, is a prostacyclin analogue which is very short acting. It lowers pulmonary vascular resistance for up to 2 hours with little effect on systemic pressures when given via aerosol. **Epoprostenol** (PGI₂) is similar in mechanism and action.

SOME IMP. NEGATIVE POINTS

- 100% Oxygen will NOT improve the cyanosis in --- TOF or intracardiac shunt.
- Alveolar-arterial oxygen gradient (A-aO₂) is NOT increased in --- Hypoventilation
- Infective Endocarditis is usually NOT seen with --- ASD
- In congenital Rubella usually NOT seen --- ASD
- Co-arcuation of aorta is NOT associated with --- PS
- Rt. axis deviation is NOT seen in --- Tricuspid atresia
- Split S₂ is NOT seen in --- Tricuspid atresia.
- S₄ is NOT seen in --- Ventricular aneurysm & AF
- Soft S₁ is NOT associated with --- Short P.R. interval
- LV hypertrophy is NOT seen in --- MS
- Aortic regurgitation is NOT seen in --- Myocardial infarction.
- Vegetations are NOT firmly fixed to valve in --- Infective/ bacterial endocarditis
- Pulsus paradoxus is NOT seen in --- IPPV
- Early diastolic murmur is NOT seen in --- Thyrotoxicosis in a old person .
- Clubbing is usually NOT seen with --- Chronic bronchitis, SCLC
- Amyloidosis is NOT seen in --- Chronic bronchitis
- Bronchiectasis is NOT seen in --- Ca-bronchus ---
- NOT seen in idiopathic pulmonary hemosiderosis --- Eosinopenia
- NOT a cause of secondary hemochromatosis --- PNH
- NOT true of acute rheumatic fever with carditis --- Trop T is elevated, myocardial biopsy shows necrosis
- NOT a cutaneous manifestation of dermatomyositis --- Salmon rash.
- NOT true about mesial temporal sclerosis --- Distinction b/w grey and white matter is lost
- NOT true about temporal lobe arteritis --- Worsens on exposure to heat
- Insulin resistance is not seen in --- Addison's disease
- Aseptic meningitis is NOT caused by --- Measles
- Pneumococcal vaccine is NOT indicated in --- Cystic fibrosis
- CSF Pleocytosis is NOT a characteristic of --- GBS
- NOT true of GBS --- Sensory level is seen characteristically
- Jaw jerk is NOT brisk in --- Myelopathy
- Hyper-reflexia is NOT seen in --- Tabes Dorsalis
- In MG NOT seen --- Absent DTR
- In SACD NOT seen --- Brisk ankle jerks
- EPS are NOT seen in --- Multiple sclerosis.
- Predominant motor neuropathy is NOT seen in --- Arsenic

intoxication, HIV

- Episodic m/s weakness is NOT caused by --- Hyperphosphatemia.
- Lateral cerebellar lesion is NOT a/w --- Resting tremors
- Pneumopathy is NOT caused by --- α -methyl dopa
- NOT a complication of IPPV --- Pleural effusion
- NOT seen in primary pulmonary HTN --- Clubbing.
- NOT a reliable diagnostic tool in pulmonary embolism --- Echo
- Riluzole is NOT used in --- T/t of hypercalcemia
- Dextroamphetamine --- is NOT given in diabetic neuropathy
- Fasting hypoglycemia is NOT seen in --- glucagon excess.
- Niclosamide --- is NOT used in neurocysticercosis
- Drug NOT useful in m/m of status epilepticus --- Carbamazepine, Lamotrigine
- **Among anti-cancer drugs :-**
 - Lung toxicity is NOT seen with --- 5-FU
 - G.I. side effect are NOT seen with --- Mtx
 - Bone marrow depression is NOT seen with --- Vincristine and L-asparaginase.
- Not seen in PAN ---- Glomerulonephritis (but renal artery stenosis can occur)
- In PAN aneurysm are NOT seen at --- extremities.
- Impaired platelet functions are NOT seen in --- ITP.
- Platelet transfusion is NOT very useful in --- ITP
- In TB Pleural effusion does NOT contains --- \uparrow mesothelial cells
- NOT a/w tuberculosis --- Xanthogranulomatous pyelonephritis
- NOT fermented by colonic flora --- Lignin
- NOT seen in Primary hyperaldosteronism --- Pedal edema
- NOT seen in sarcoidosis --- Osteomalacia, adrenal involvement
- Pseudotumour cerebri is not seen with --- Gentamycin
- **Gynecomastia is NOT seen with**
 - SCLC (*Seen with large cell adeno Ca. of lung*)
 - Sarcoidosis.
- **Hypercalcemia is NOT seen in**
 - Acute pancreatitis, Celiac d/s
 - Myositis ossificans progressiva
 - Tumour lysis syndrome
 - Phenytoin therapy
- NOT true about hyperaldosteronism (Conn's syndrome) --- Metabolic acidosis
- Hypokalemia is NOT seen in --- ARF & CRF
- In Hyponatremia NOT seen --- Periodic paralysis

- In alcoholism NOT seen --- Polycythemia
- Plasmapheresis is NOT used in --- Cholinergic crisis
- Peptic ulcer is NOT seen in --- Pernicious anemia, PV syndrome.
- NOT included in WHO criteria of polycythemia vera --- High LAP score.
- Hepatomegaly is NOT seen in --- Hepatic porphyria
- Anti-phospholipid syndrome is not a/w --- Pancytopenia
- Lupus like syndrome is NOT caused by --- Penicillin
- NOT seen in sarcoidosis --- Lung cavitation
- NOT a cause of Charcot's joint --- Poliomyelitis
- NOT true about pseudogout --- Involves small joints
- NOT true of gouty arthritis --- 90% cases are d/to uric acid overproduction
- Fibrinolytic (thrombolytic) therapy is NOT beneficial in --- NSTEMI
- Midline granuloma are NOT a/w --- Sjogren syndrome
- Pulmonary hypertension is NOT seen in --- Pulmonary stenosis
- Uncontrolled hypertension is NOT a/w increased risk of --- DM
- Spastic paraplegia is NOT seen in --- Lead poisoning
- NOT a cardiac manifestation of HIV --- Aortic aneurysm
- NOT a cause of systolic thrill in ICS 2nd and third --- Ebstein's anomaly
- Hirsutism is NOT caused by --- Hyperthyroidism
- B/L medullary nephrocalcinosis is NOT seen in --- Autosomal Recessive PKD
- NOT seen in right cerebral hemispheric lesion --- Dysgraphia
- NOT seen in HIV positive pt --- Inclusion body
- Congenital hypercoagulability is NOT seen in --- Antiphospholipid syndrome
- NOT seen in Antiphospholipid syndrome --- Bleeding disorders
- Joint NOT involved in RA --- Tarsometatarsal joint
- Joint of hands are NOT involved in --- AS.
- NOT a cause of Horner's syndrome --- Medial medullary syndrome.
- NOT a marker of active replicative phase of chronic hepatitis B --- Anti HBc
- NOT true of metachromatic leukodystrophy --- Involves deep cortical neurons
- NOT a major Framingham Criteria for d/g of CHF --- Hepatomegaly.
- NOT a feature of medullary cystic kidney or nephroptysis --- Nephrocalcinosis (Stones in kidney).
- NOT true about antigen detection in malaria --- Detects

- aldolase antigen
- Granulomatous vasculitis is NOT seen in --- Buerger's d/s
 - NOT a test for DM --- D- xylose
 - NOT included in Jone's Major criteria --- High ESR
 - NOT true of sub-endocardial hemorrhages --- Involves RV wall.
 - Respiratory depression is NOT caused by --- Strychnine.
 - NOT recommended in patients of nephrocalcinosis --- Calcium restriction.
 - NOT recommended in t/t of hypercalcemia without ECG changes --- Calcium gluconate
 - Drug NOT useful in preventing contrast nephropathy--- fenoldopam.
 - NOT an autoimmune d/s --- Sick cell d/s
 - NOT true of DM --- Patient with type 2 DM never requires insulin
 - Drug NOT used in migraine prophylaxis --- Levitiracetam

CLINICAL VIGNETTES

- A 36 year old chronic smoker with emphysema presented to casualty with breathlessness and dyspnoea at rest. O/E there is pedal edema, tender hepatomegaly and b/L rales on auscultation all over chest. His BP is 136/86 mmHg. Most likely diagnosis is

[DNB HRH Delhi 2008]

- A. LVF
- B. CHF
- C. Cor pulmonale
- D. COPD

(Ans: C. Cor pulmonale)

Features are s/o right sided heart failure secondary to chronic lung d/s. Rt heart failure secondary to lung d/s is k/as cor pulmonale

- A 12 year old girl presents with pain and swelling in her right knee joint. Movements are restricted. Other joints are normal. All of the following c/b considered in d/d of this

condition except-- [DNB HRH Delhi 2008]

- A. TB
- B. Hemophilia
- C. Septic arthritis
- D. JRA

(Ans: B. Hemophilia)

- Hemophillia is XR disorder and it manifests in boys.

- A 42 year old female complaints of fatigue and weakness. Laboratory findings reveal hypercalcemia, and PTH is undetectable in blood. Most likely diagnosis is

[DNB MAMC, Delhi 2008]

- A. Adrenal insufficiency
- B. Hypoparathyroidism
- C. Hypothyroidism
- D. Hypopituitarism

(Ans: A. Adrenal insufficiency)

There are only few conditions which are a/w hypercalcemia and undetectable PTH---

- Malignancy related hypercalcemia is also a/w undetectable PTH., hypercalcemia. Thyroid carcinoma is an example
- Jensen's d/s is a rare inherited d/s of childhood char/by multiple developmental defects of skeleton, hypercalcemia, hypophosphatemia and undetectable levels of PTH.
- In 10 to 20% cases of adrenal insufficiency there is hypercalcemia. PTH levels may be undetectable.

- A female presents with goitre. Laboratory findings reveal high TSH and low T4. Most likely diagnosis is

[AIPGMEE 2011]

- A. Hashimoto thyroiditis
- B. Hypoparathyroidism
- C. Grave's d/s
- D. Pituitary tumour

(Ans: A. Hashimoto thyroiditis)

Autoimmune hypothyroidism is a/w Hashimoto's thyroiditis and atrophic thyroiditis in later stages.

TFTs in the above mentioned diseases

	FT4	TSH	Remark
Hashimoto's	↓	↑	Female > M
Reidel's	↓	↑	
Graves' d/s	↑	↓↓	
Pituitary d/s			Variable

- A 7 year old child presents with complaints of abdominal pain and red urine. He is hypertensive and also has neuropathy. Most likely d/g is

[DNB MAMC Delhi'08]

- A. Glomerulonephritis
- B. Acute intermittent porphyria
- C. Ureteric colic
- D. Lead intoxication

(Ans: B. Acute intermittent porphyria)

- A girl on sulphonamides develops pain abdomen and presents to the emergency department with seizures. Most likely d/g is

[AIIMS Nov '2008]

- A. Congenital erythropoietic porphyria
- B. Acute intermittent porphyria
- C. Infectious mononucleosis
- D. Kawasaki d/s

(Ans. B. Acute intermittent porphyria)

AIP (Acute intermittent porphyria) is an important cause in of pain abdomen. It is precipitated by certain drugs most commonly by sulfonamides. Neuropsychiatric manifestations including neuropathy, seizures are common

- A 42 year male was admitted for # shaft of femur. During surgery he develops altered sensorium and dyspnoea on OT table. His end tidal CO_2 is decreased to zero. Most likely cause of his condition is

[DNB HRH Delhi'08]

- A. Compartment syndrome
- B. Malignant hyperthermia
- C. Fat embolism
- D. Venous air embolism

(Ans. C. Fat embolism)

- **Fat embolism** is common after long bone # esp shaft of femur, usually seen 12 to 72 hours after #, Et CO_2 levels fall to zero
- **Venous air embolism** is common during surgery above the level of heart (of head/neck region) esp in sitting position. Usually seen during surgery. Signs are unexplained hypotension, tachycardia and sudden decrease in Et CO_2 levels
- **Malignant hyperthermia** is a complication of volatile fluorinated anaesthetics. There is hyperpyrexia, tachycardia, m/s rigidity, hypertension. Increased Et CO_2 levels.

- A patient developed breathlessness and chest pain, on second post op day of THR. ECHO revealed right ventricular dilatation and TR. Most likely cause is

[AIPGME'10]

- A. Acute MI
- B. Hypotensive shock
- C. Pulmonary embolism
- D. Cardiac tamponade

(Ans. C. Pulmonary embolism)

- Acute MI is uncommon as there is neither risk factor mentioned nor there is characteristic pain.
- Features of shock are not mentioned, so option B is unlikely
- Right ventricular dilatation and TR are s/o right heart failure. Pulmonary embolism can lead to very high

pulmonary artery pressure and right heart failure.

- Cardiac tamponade will lead to raised JVP and very high filling pressures, decreased cardiac output.
- So, the best answer is C

- An 18 year old male presented with acute onset of descending paralysis of 3 days duration. There is a h/o blurring of vision. Patient has quadriparesis with areflexia. both pupils are non-reactive. Most probable diagnosis is

[DNB HRH Delhi'08]

- A. Paralytic poliomyelitis
- B. Post-diphtheric paralysis
- C. Botulism
- D. GBS

(Ans. B. Post-diphtheric paralysis)

- GBS is ruled out as there is no ascending paralysis
- Paralytic poliomyelitis is ruled out as there is acute asymmetric ascending paralysis seen in GBS.
- In Botulism --- Onset of paralysis is usually seen b/w 1-3 days. It is characterised by descending paralysis, blurring of vision (pupils are dilated, diplopia, loss of accommodation). Patient has flaccid paralysis. Reflexes may be normal or decreased.
- Post-diphtheric paralysis --- Features are similar to botulism. Onset of paralysis is seen late (b/w 1-8 weeks). It is characterised by acute descending symmetrical quadriplegia, blurring of vision (**ophthalmoplegia**, loss of accommodation, pupils are non-reactive) and areflexia.

- A 60 year old male presents with progressive dementia for past 6 months with intermittent jerky movements of whole body from 2 days. EEG showed sharp bipolar spikes. Most likely diagnosis in this patient is ?

[AIIMS Nov'10]

- A. Alzheimer's d/s
- B. Creutzfeld-Jacob d/s
- C. Lewy body d/s
- D. Herpes simplex encephalitis

(Ans. B. Creutzfeld-Jacob d/s)

Intermittent involuntary jerks are myoclonus

- **CJ disease** typically presents with progressive and profound dementia + myoclonus + sharp bi/triphasic spikes in EEG in elderly (50-75 yr).
- **Lewy body disease** typically presents with subacute dementia with delirium, myoclonus and extrapyramidal symptoms.
- **Alzheimer's dementia** is seen in elderly usually >65 yrs. Typically presents with subacute dementia with delirium, myoclonus and extrapyramidal symptoms.

- Dementia + myoclonus may be seen in ---

Alzheimer's dementia, Lewy body dementia, cryptococcal encephalitis, myoclonic epilepsy disorder.

- ❑ A 9-year-old boy begins to have difficulty walking. His condition gradually worsens, and his difficulties with coordination slowly spread to his arms and trunk. Physical examination is notable for an ataxic gait and nystagmus. All reflexes (ankle & knee jerk) are absent and only extensor reflex (plantar extensor) is present. What is the diagnosis? [AIPGMEE'2012]

- (A) Subacute combined degeneration of spinal cord
- (B) Amyotrophic lateral sclerosis
- (C) Becker's Dystrophy
- (D) Friedreich's ataxia

(Ans. (D) Friedreich's ataxia)

See the table : D/d of ALS, SCD, & Friedrich's ataxia in the medicine: CNS section.

- ❑ A 29 year old male, who was on oral hypoglycemics and never had ketonuria in his life, presents with high RBS. His grandfather had diabetes and his father who is the only son of his grandfather, did not have the disease. The type of DM the person can never have is

[AIPGMEE'2009]

- A. Pancreatic DM
- B. MOD of young
- C. Type I DM
- D. Type II DM

(Ans. C. Type I DM)

Family history and HLA association is strongly positive in Type I DM. Further its onset is in childhood (juvenile DM), DKA is a frequent c/c

- ❑ An 76 year old lady with #NOF 1 mo back, presents with 2 days h/o altered sensorium and decreased urine output. Her s. urea is 140 mg%, Cr is 2 mg% and serum calcium is 15.5 mg%. Which of the following is NOT useful in immediate m/m. [AIIMS Nov' 2010]

- A. Furosemide
- B. Hemodialysis
- C. Normal saline
- D. Biphosphonates

(Ans. D. Biphosphonates)

Biphosphonates are contraindicated in presence of deranged KFT, peptic ulcer and esophageal dysmotility.

- ❑ A 7 year old girl with end stage renal disease requiring hemodialysis presents with proximal m/s weakness. Her

K⁺ is 7.8 meq/L. EKG is showing peaked tall T-waves. Which of the following will lower her K⁺ most quickly?

[AIPGMEE'2009; May' 2010]

- A. Calcium gluconate intravenously
- B. Glucose and insulin
- C. Kayaxalate resins
- D. Intravenous sodabcarb

(Ans. A. Calcium gluconate intravenously)

- T/t options for acute severe hyperkalemia include :

1. I/v Ca- gluconate either as bolus or as infusion. It efficiently lowers serum K⁺ levels as well as it decreases membrane excitability. This membrane stabilizing action would be beneficial to control arrhythmias.

2. I/v glucose and insulin infusion combination acts rapidly by shifting K⁺ into cells.

- K⁺ binding resins are used to treat chronic hyperkalemia

- I/v Sodabcarb (alkali therapy) is contraindicated in presence of CRF. It is used judiciously only for severe hyperkalemia a/w metabolic acidosis.

- ❑ Diabetic patient with blood glucose of 600 mg/dL and Na⁺ 122 mEq/L was treated with insulin. After giving insulin the blood glucose decreased to 100 mg/dL. What changes in blood Na⁺ level is expected-

[AIPGMEE'2003; CG'2009]

- A. Increased Na⁺ level
- B. Decreased Na⁺ level
- C. No change would be expected
- D. Na⁺ would return to previous level spontaneously on correction of blood glucose

(Ans. A. Increased Na⁺ level)

Due to osmotic flux of water from ICF to ECF extracellular Na⁺ will be low and reverse occurs when correction is done.

As plasma glucose decreases by

100 mg% sodium tends to increase by 1.6 mEq/L.

- ❑ A 40 yr old lady presents with temporal field defects and galactorrhea. The most likely cause is

[AIPGMEE'2009]

- A. Pituitary macroadenoma
- B. Craniopharyngioma
- C. Pregnancy
- D. Lactation failure

(Ans. A. Pituitary macroadenoma)

- A 55 years old diabetic woman without any previous h/o headache presented with severe acute headache, nausea and on examination there was neck rigidity. There was also past h/o photophobia. M/c cause can be ---

[AIIMS May '2009]

- A. Acute viral encephalitis B. Hydrocephalus
C. Migraine D. SAH

(Ans. D. SAH)

- A patient presents with thunderclap headache f/b unconsciousness with progressive oculomotor nerve palsy. M/c cause can be ---

[AIIMS Nov '2010]

- A. EDH B. Hydrocephalus
C. Basilar migraine D. Aneurysmal SAH

(Ans. D. Aneurysmal SAH)

Aneurysmal SAH

The moment aneurysm ruptures, the ICP rises suddenly and there is **sudden** transient loss of consciousness, which may be preceded by brief severe/excruciating headache. Sudden onset is characteristic. Sometimes the pt describes worst headache of my life. FND may occur e.g. 3rd CN palsy.

Cluster headache

Rare headache c/by deep, retroorbital pain excruciating headache. Periodicity is characteristic. A/w autonomic ipsilateral symptoms- lacrimation, rhinorrhea, ptosis but there is no 3rd CN palsy.

Basilar Migraine (vertebrobasilar migraine)

Basilar or brain stem symptoms (vertigo, ataxia, dysarthria, or diplopia) are present. Symptoms last usually in 10 to 30 minutes f/b headache.

Uncommon in adults >50 and in children. Recovery is spontaneous.

Ophthalmoplegic Migraine

Recurrent unilateral headaches a/w weakness of extraocular m/s. A transient oculomotor nerve paralysis may be seen.

- A male presented with sudden onset of thunder clapping headache, unconsciousness, vomiting. What is the most probable diagnosis?

[AIIMS Nov'09]

- A. Acute ischemia of midbrain
B. Acute aneurysmal hemorrhage

- C. Meningitis
D. Tubercular lesion

(Ans. Acute aneurysmal Hemorrhage)

Thunder clapping headache is a variant of migraine which simulates SAH. Head trauma and aneurysmal rupture are important causes of SAH. D/d of a primary thunderclapping headache with sudden onset include --- sentinel bleed from intracranial aneurysm, cervicocephalic arterial dissection, and cortical venous thrombosis. So most appropriate option is B.

- A 23 yr old female presented with headache, vomiting, tinnitus, and vertigo. Her mother also has headache. Most probable diagnosis?

[AIPGMEE'11]

- A. Basilar migraine B. Cervical vertigo
C. Vestibular neuronitis D. Multiple sclerosis

(Ans. Basilar migraine)

- Female presented with occipital headache. Mother also had similar history. Most probable diagnosis?

[AIIMS Nov'09]

- A. Basilar migraine B. Vertigo
C. Vestibular neuronitis D. Occipital lobe tumor

(Ans. Basilar migraine)

Basilar migraine is c/by dysarthria, diplopia, vertigo. Neurological symptoms are f/b throbbing occipital headache. Family history is positive in some patients.

- A patient known to have mitral stenosis and atrial fibrillation, presents with acute onset of weakness in the left upper limb which recovered completely in two weeks. The most likely diagnosis is

[AIPGMEE'10]

- A. Transient ischemic attack B. Ischemic stroke
C. Hemorrhagic stroke D. Vasculitis

(Ans.: A. TIA)

MS with AF patients are at risk of thromboembolic episodes, microembolization which can lead to TIA.

- A 28 years old female presented with Butterfly rash on the face. Laboratory findings revealed hemoglobin of 8 mg%, leucocyte count 1000/L and platelets 80,000/L. Which of the following antibody if found in patient's blood would best yield the diagnosis?

[AIPGMEE'2012]

(A) Anti-dsDNA Antibodies

- (B) Anti centromere Antibodies
- (C) Anti-CCP Antibodies
- (D) Anti phospholipid Antibodies
- (Ans. (A) Anti-dsDNA Antibodies)

Clinical findings of butterfly rash in a young female supported by lab evidence of anemia, thrombocytopenia, leucopenia are s/o SLE. Anti-dsDNA Antibodies are most specific for SLE. Anti-CCP Antibodies are specific for RA.

- A young girl presents with pain at the tip of fingers of the hand and further mentions that the pain worsens & becomes severe on exposure to cold. What is the most likely diagnosis? [AIPGMEE'12]

- A. Sausage digits
- B. Purpuric lesions on the hands
- C. Hardening of finger
- D. Pallor of finger pulp

(Ans. A. Sausage digits)

Symptoms are typical of Raynaud's phenomena which is seen in scleroderma. Scleroderma is c/by calcinosis cutis, Raynaud's phenomena, Esophageal dysmotility, Sclerodactyly (Sausage digits), Telangiectasias, all together k/as CREST syndrome.

- A 40 yr old female presents with rashes on both lower limbs and arthralgia in knee joints. On serum electrophoresis of proteins monoclonal and polyclonal cryoglobulins were found. What is the most likely etiology?

[AIIMS May' 2010]

- A. HBV
- B. EBV
- C. HCV
- D. Parvo virus

(Ans. C. HCV)

Cryoglobulinemia or EMC (essential mixed cryoglobulinemia) was initially reorted with HBV infection. EMC is c/by arthritis, palpable purpura (cutaneous vasculitis), and occasionally GN and circulating immune complexes of polyclonal immunoglobulin classes. Many patients have associated chronic liver d/s. The association with HBV infection is limited; instead a substantial proportion has chronic HCV infection, with circulating immune complexes containing HCV RNA.

- A 70 yr patient with anti hepatitis C antibodies positive is admitted has renal dysfunction. He has few skin rashes and

ulcerations. What is the likely diagnosis?

[AIPGMEE' 2012]

- (A) MPGN
- (B) Mixed Cryoglobulinemia
- (C) Alport's syndrome
- (D) HUS
- (Ans. (B) Mixed Cryoglobulinemia)

See explanation in prev. qn.

- A lady with back pain, hyperpigmentation palms & soles with back pain, urine showed green color and black sediment with benedicts test, intervertebral disc calcifications. Most probable diagnosis is

[AIIMS May' 10]

- A. Alkaptonuria
- B. Phenylketonuria
- C. Tyrosinemia type 2
- D. Arginosuccinic aciduria
- (Ans. Alkaptonuria)

See explanation in pedia section

- A young female presented with intermittent ptosis, proximal muscle weakness and a fatigability. Which is the best diagnostic investigation?

[AIIMS Nov'09]

- A. Edrophonium Test
- B. Muscule Biopsy
- C. CPK
- D. Electromyogram

(Ans. Electromyogram)

Clinical features are typical of MG. Female sex, proximal m/s weakness, ptosis are points in support of d/g. Single fibre EMG is confirmatory. Edrophonium test is simple diagnostic test.

- A 29 yr old female patient with limited scleroderma and one month history of shortness of breath was found to have the following measured parameters on PFT :-- FEV₁ 80% (expected 88%), FVC 84% (expected 80%), DLCO 55% (expected 100%)

[AIIMS Nov'09]

- A. Interstitial lung disease
- B. Pulmonary HTN
- C. Bronchiectasis
- D. Diaphragmatic weakness

(Ans. Pulmonary HTN)

Pulmonary hypertension is common in patient with limited scleroderma patient. It manifests as dyspnoea and PFT are usually dearranged. PFT in qn are significantly ↓ DLCO, slight ↑ FVC, slight ↓ FEV₁

PFTs in various Pulmonary d/s

	FVC	FEV ₁	DL _{CO}	Remark
ILDs	↓	↑	↓	Parenchymal restrictive d/s
Pulmonary HTN	↓	↑	↓	C/b seen in pulmonary fibrosis
Bronchiectasis	↓	↓↓	N	Obstructive lung d/s
Diaphragmatic weakness	↓	↑	↓	Extraparenchymal restrictive d/s

ILDs may have similar PFT but most ILDs have chronic or subacute presentation. FVC is also reduced in ILDs.

- 29 year old male truck driver presents with h/o fever, loss of weight of 10 kg, white lesions in oral mucosa and difficulty in breathing. On CXR PA view b/L infiltrates were present. Most likely cause of breathlessness is ---

[AIPGMEE'10]

- A. Candidiasis
 - B. Pneumocystis Carinii
 - C. Pulmonary tuberculosis
 - D. Mycoplasma pneumoniae
- (Ans. B. Pneumocystis Carinii)

Clinical picture is typical of HIV disease. Acc/to WHO any individual is considered to have AIDS if atleast 2 of major signs are +nt with one minor signs:

• **Major signs :**

- Weight loss > 10% of body weight
- Chronic diarrhoea > 1 month
- Persistent fever for > 1 month

• **Minor signs :**

- Generalized pruritic dermatitis
- Persistent cough > 1 month
- Herpes zoster
- Disseminated HSV infection
- Oropharyngeal candidiasis
- Generalised lymphadenopathy

Pneumocystis Carinii is the m/c cause of pneumonia in AIDS patient. D/g is further supported by CXR finding of b/L infiltrates.

- A patient presents with fever of 3 weeks and splenomegaly. Blood culture reveals foci of hypoechoic lesions in the spleen. Blood culture reveals Gram negative organism. Most probable organism implicated is:

[AIPGMEE'10]

- A. CMV
- B. Salmonellosis

C. Tuberculosis

D. Malaria

(Ans.: B. Salmonellosis)

Long duration fever and splenomegaly are s/o either malaria or enteric fever caused by salmonella. USG abdomen is showing hypoechoic lesions which are d/to splenic abscesses c/by salmonella. Gram negative organism on blood culture further supports d/g.

- A T3 complete paraplegic patient present with complaint of severe headache. O/e he is having BP of 210/120 with paradoxical bradycardia at 56 bpm. He should be treated with . [AIPGMEE'12]

- A. Cortico-steroids
- B. Nimodipine
- C. IV Ringer Lactate
- D. Inj. subcutaneous heparin

(Ans.: B. Nimodipine)

The patient is having hypertension with raised ICT → headache → bradycardia, features typical of cushing's reflex. There is a risk of SAH. Mild hyperventilation, mannitol, sedation and analgesia is preferred. Measures to ↓ ICT are used. Nimodipine prevents ischemic injury.

- A patient presents with symptoms of hypoglycemia. Investigation reveals low RBS and high insulin levels, C-peptide assay is normal. The most likely diagnosis is:

[AIPGMEE'10]

- A. Insulinoma
 - B. Accidental ingestion of sulphonylureas
 - C. Accidental exogenous insulin administration
 - D. Accidental metformin ingestion
- (Ans.: D. Accidental metformin ingestion)

D/d of hypoglycemia d/to

	Insulin	Pro-insulin levels	C-Peptides	Remark
Insulinoma	↑	↑	↑	Suspected in pt with f/h of MEN I
Exogenous insulin	↑	N	↓	Fasting hypoglycemia
Exogenous SU	N	N	↑	Fasting hypoglycemia
Exogenous biguanides	↑	N	N	Fasting hypoglycemia

[Photographs in SVD section :
Courtesy Dr. Shail Gupta MD (Dermatology)]

ANATOMICAL & PHYSIOLOGICAL CONSIDERATION

Morphology of skin

- Skin is composed of Epidermis --Dermis ---Subcutaneous tissue from outer to inner
- Epidermis is composed of 5 layers.

1. *Stratum corneum* (spinous/ horny layer)

Outermost cornified or horny cell layer. Thickest on the palms and soles and thinnest on the eyelids and the prepuce. This layer is underdeveloped in VLBW newborns. Ringworm lives in this layer.

2. *Stratum lucidum* :

Stratum lucidum is also present as an interim layer and is responsible for transparency. Present only in palms and soles.

3. *Stratum granulosum* (granular layer)

Contains filaggrin, basophilic keratinohyaline granules.

4. *Stratum spinosum*/ Prickle / Malpighian layer (spinous layer)

Occupies most of the epidermis. Contains desmosomes, langerhans cells

5. *Stratum germinativum* (basal layer)

Contains mitotically active keratinocytes, melanocytes. Acantholytic cells in pemphigus vulgaris are derived from stratum basale.

- Dermis is composed of collagen, elastic fibers, sweat/sebaceous glands. It contain

1. Papillary dermis

Lies immediately beneath the epidermis

2. Reticular dermis

Involved in bulla formation in burns

- Normal turnover time for epidermis : 4 weeks (28 days)
- Ringworm lives on stratum corneum layer.
- *Stratum basale & spinosus* synthesize vitamin 7 -dehydrocholecalciferol (Pro-vit D).
- Dx of keratosis is made by skin scrappings.

SOME DIAGNOSTIC METHOD

Tests

- Tzanck Smear ---Useful in diagnosis of herpes lesions (HSV / VZV multinucleate giant cells)
- * Tzanck test ---Used to differentiate viral lesions of skin from pemphigus.
- Patch test ---For contact dermatitis (test is read after 48 hours).

WOOD LAMP'S LIGHT

W~ is made up of nickel oxide & silica. It generates 360 nm UV- A light (black) :-

- *Corynebacterium minutissimum* (erythrasma)--- Coral red color
- * *Pseudomonas*, *psoriasis*--- Pale blue.
- Tuberous sclerosis --- Ash leaf spots[blue white]
- Vitiligo --- Chalky white
- * *Porphyria cutanea tarda* --- pinkish red (urine)
- Tinea versicolor --- Golden fluorescence
- Tinea capitis (*M. Canis*) --- Yellow fluorescence
- SqCC --- Red fluorescence

* Fungi which give fluorescence in wood's light are :- *M. Canis*, *M. audouinii*, *T. schoenleinii*

→ Maltese crosses are seen on polarizing histological sections containing the fungi of --- *Penicillium marneffi*, *cryptococcal spores*.

→ KOH preparation : Used for D/g of Tinea infections

* Patch test : Read after 2 days

Diascopy

- Hemangioma ---- Blanches with pressure
- Granuloma --- Apple jelly appearance

Köbner's isomorphic phenomena

Traumatized area often develops lesions especially over elbow

knee. Seen in ---

- o Psoriasis
- * Lichen planus, lichen nitidus, lichen sclerosus
- o Vitiligo
- o Kaposi sarcoma
- ✓ Pityriasis rubra pilaris
- ✓ Necrobiosis lipoidica

Pseudo-isomorphic phenomena is seen in : Pityriasis Rubra Pilaris (PRP), molluscum contagiosum, warts.

* Pathergy is a similar response seen in pyoderma gangrenosum and Adamantiades-Bechet's syndrome.

Nikolskiy's sign

- o Is peeling-off of clinically normal skin away from lesion by gentle pressure d/to acantholysis.
- o Seen in intra-epidermal bullae & when d/s is active. E.g.
 - Pemphigus
 - Staphylococcal scalded skin syndrome (SSSS)
 - TSS
 - Porphyria
- o *Pseudo-Nikolskiy's sign* is peeling-off of skin d/to apoptosis (necrosis) . It is seen in : TEN, SJS, erythema multiforme.
- * Pear sign is collection of fluid in lower part of blister cavity. It is seen in intraepidermal flaccid bulla e.g. Pemphigus
- * Bulla spread sign is extension of blister in direction opposite to side of pressure. Spread with sharp edge is seen in pemphigus while spread with rounded edge is seen in BP.
- * Sheklakov sign is pin point bleeding spot on peeling -off of the remnant of blister. Seen in subepidermal bulla e.g. BP, EBA.
- o *Auspitz sign* is punctate bleeding spot on peeling -off of the membranous scales. Characteristically seen in psoriasis.

	Intra/e bulla	Sub/e bulla	Clinical conditions
1. Nikolskiy's sign	+	-	Pemphigus, SSSS
2. Pseudo Nikolskiy's sign	+		TEN, SJS, EM
3. Pear sign	+	-	Pemphigus
4. Bulla spread sign (Asboe-Hansen's)	+	+	Sharp edge: Pemphigus Rounded edge: BP
5. Sheklakov's sign	-	+	BP, Epidermolysis bullosa acquisita

CONFIGURATION OF LESION

- o Annular : Ringworm, pityriasis rosea, leprosy, secondary syphilis, granuloma annulare.
- o Linear : Lichen planus, warts, sporotrichosis
- o Grouped : Herpes, dermatitis herpetiformis.
- o *Involvement of dermatomes is seen in :*
Herpes zoster.
- o *Painful lesions are seen in :*
Herpes infection.
- * Painless lesions are seen in :
Dermatitis herpetiformis (itchy lesions), pemphigoid, pemphigus, erythema multiforme.
- o Sub-epidermal lesions are seen in :
Dermatitis herpetiformis, pemphigoid, erythema multiforme.
- o Intra-epidermal lesions are seen in :
Herpes, pemphigus
- ✓ Lesions involving oral mucosa are seen in :
Secondary and congenital syphilis, pemphigus, Peutz Jegher syndrome, Lichen planus.
- o Umbilicated bullae are found in :
Pox (molluscum contagiosum).

PAPULAR LESIONS/WARTS

Warts (verrucae)

Verruca	◦ M/c type
vulgaris /	◦ Dorsum of hand / finger is m/c site
Common warts	* A/w HPV 2 & 4
	◦ Kobner's phenomena is seen
	◦ T/t: Electrodesiccation/ podophyllin
Myrmecia W~	* Painful deep plantar warts
(Verrucus verruca)	◦ Dome shaped papule
	* A/w HPV 1
Condyloma acuminata	◦ Cauliflower like growth in genitalia
(venereal warts)	* Koilocytes ⁺
	* A/w HPV 16 and 11
	◦ Common in sexually promiscuous young adults
	◦ Usually not premalignant but Buschke-Löwenstein variant is precancerous

- In warts there is hyperplasia of all layers of epidermis + acanthosis + papillomatosis.
- Buschke Lowenstein tumour is precancerous verrucous tumour d/to HPV 16,18.

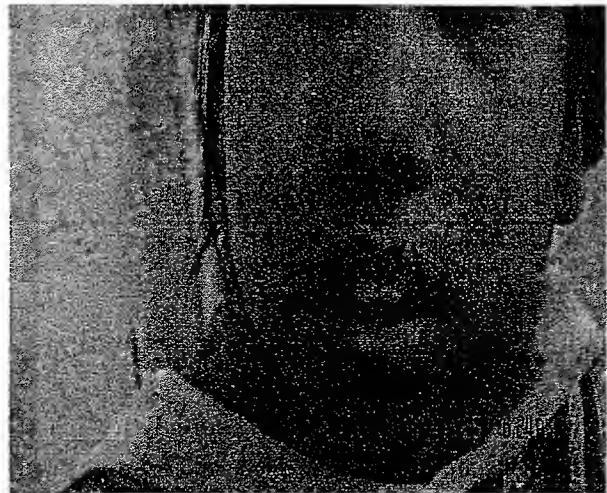


Photograph : Genital warts

- HPV infects squamous epithelium of both keratinized stratum corneum & non keratinized surface by direct inoculation.
- * Wart paints are most effective in condyloma acuminata, in plantar/filiform warts of scalp and beard region.
- Podophyllin is contraindicated in pregnancy & Cryo/laser is TOC for anogenital warts in pregnancy. Trichloroacetic acid cautery is also useful.

Molluscum Contagiosum

- D/to infection with pox virus. School children are affected.
- * Extra-genital molluscal lesions are marker of AIDS in adults.
- * M/c type MCV-1.
- M/c prevalent type MCV-2, responsible for adult STDs.
- Umbilicated papules (fleshy /pearly white multiple papules) are characteristic. Pruritic lesions are seen over face, trunk, genitals.
- Henderson-Peterson bodies (HP bodies) are seen which are intracytoplasmic inclusions in epidermal cells
- * Self limiting d/s. T/t --- Curette small lesion or cauterization using 20-30% trichloroacetic acid.



Photograph : Molluscum contagiosum

- Darrier white d/s is AD d/s c/by warty papules & plaques in seborrheic sites. Histology shows suprabasal acantholysis in epidermis & dyskeratotic cells.
- * Dowling Degos d/s is AD genodermatosis.

VESICO-BULLOUS DISORDERS

IMPETIGO

- * M/c bacterial skin infection of children. M/c site is face.
- M/c cause is staphylococcus aureus.
- Honey colored crusts are seen.
- * Ecthyma is a variant of impetigo seen in lower limbs and causes punched out ulcerative lesions.
- * Staphylococcal scalded skin syndrome (SSSS) is also k/ as Ritter's d/s or pemphigus neonatorum.
- T/t: Debridement.

	Non-bullous (contagiosa)	Bullous
Age group	Pre-school/ young children	Newborn
Organism	Strepto. pyogens, staph	Staph. aureus gpII
Clf	Yellow brown "honey colored crusts"	Vesicles/ bullae 2-3 cm in diameter, subside in 2-3 days

Causes of bullae / Vesicles

Intra epidermal	Sub-epidermal	Intra-epidermal or sub-epidermal
- Pemphigus	- Bullous pemphigoid	✓ Erythema multiforme
- Contact	- Herpes gestationalis	✓ TEN
- SSS syndrome (staphylococcal)	- Dermatitis herpetiformis	✓ Bullae in diabetes
- Bullous impetigo	* Linear IgA disease	
- Herpes	* Hemodialysis	
- VZV	* Cutaneous emboli	
	* Porphyria variegata	

* In burns sub-epidermal supra basal bullae are seen (in superficial dermis.)

Bullous PEMPHIGOID (Senile pemphigoid)

- Sub-epidermal blisters.
- ✓ Blisters/Bullae are tense, **non-acantholytic**, rich in eosinophils are found on an erythematous or urticarial background.
- * Elderly >60 year affected. Lower abdomen is common site.
- Linear IgG auto-antibodies are formed against **hemi-desmosome (basement membrane)**. Complement C₃ is deposited. Antigen is deposited in lamina lucida.
- Bulla regenerates (Nikolsky sign is -ve). No scar is left behind the blister (**Healing without scarring**).
- T/t : prednisolone in low doses

PEMPHIGUS

- Autoimmune d/s of skin and mucosa c/by intra-epidermal / vesico-bullous lesions
- Presence of IgG circulating antibodies Vs. Keratinocyte (cement substance of skin & mucosa).
- ✓ White lace like/streak like lesions usually start in oral mucosa. Painful erosions/ recurrent ulcerations are present.
- Bulla appears in crops on apparently normal skin and m/m.
- A/w HLA-A 10 & HLA-DRW4
- Nikolsky's sign +ve

- ✓ D/g by **TZANCK TEST**, Fish-net pattern of IgG in epidermis in direct immunofluorescence
- ✓ Intraepidermal acantholysis is demonstrated in Tzanck smear (loss of cohesion between epidermal cells).
- T/t : fluids, nicotinamide, steroids.

- | | |
|-------------|--|
| P. vulgaris | <ul style="list-style-type: none"> ◦ M/c type ◦ Non-pruritic ✓ Earliest change is <u>supra-basal acantholysis</u> ◦ M/c type * <u>Worst P/g</u> |
|-------------|--|

- | | |
|-------------|--|
| P. vegetans | <ul style="list-style-type: none"> ✓ Rarest variety ◦ Supra basal * <u>Eosinophilic abscess</u> ◦ <u>Most superficial bullae</u> |
|-------------|--|

- | | |
|--------------|---|
| P. foliaceus | <ul style="list-style-type: none"> ◦ <u>Scaly, crusted erosion</u> * <u>Subcorneal bullae</u> with acantholysis (granular layer) or higher in epidermis |
|--------------|---|

- | | |
|------------------|--|
| P. erythematosus | <ul style="list-style-type: none"> ◦ Face ✓ <u>Sub-corneal</u> |
|------------------|--|

Paraneoplastic pemphigus

A/w some neoplasms like NHL, CLL, Waldenstrom's macroglobulinemia, thymoma, spindle cell tumour and Castleman d/s

Pemphigoid gestationis/ Herpes gestationis

- ✓ Non-viral, sub-epidermal blistering d/s of pregnancy and puerperium. Polymorphic erythematous papules and plaques or frank bullae are found. IF studies show linear deposits of C3

DERMATITIS HERPETIFORMIS

- Chronic, recurrent, papulovesicular d/s with intense pruritus⁺⁺⁺
- * Bilateral symmetrical lesions appear in crops over extensor joint surfaces (knee, elbow, sacral, scalp, axilla, shoulder, buttocks).
- A/w HLA-B₈ or DRW₃
- C₃ and granular IgA deposits in dermal papillae
- Biopsy : Sub-epidermal bullae and supra-papillary micro-abscesses are formed.
- A/w
 - Abnormal thyroid function
 - Achlorhydria/ Anti-parietal cell antibodies/Atrophic

gastritis

* Gluten sensitive enteropathy (Coeliac sprue).c T/t : Dapsone is DOC. Gluten free-diet is advised.

**

Histological /F of Bullous (blistering) lesions

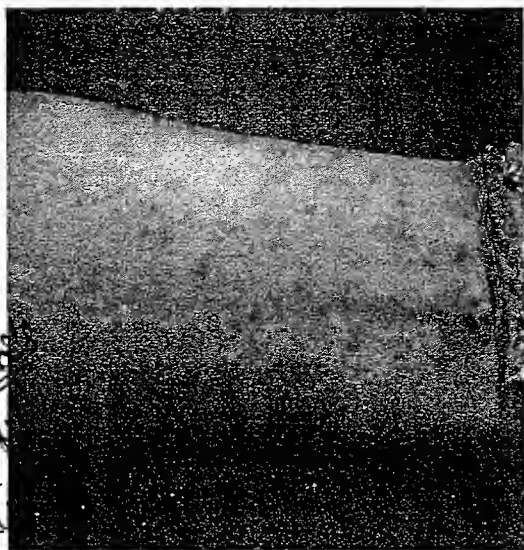
D/s	Histology	Immunofluorescence
Pemphigus vulgaris	Acantholytic lesions suprabasal blisters	Fish-net pattern of IgG in epidermis/keratinocytes
Pemphigus foliaceus	Blister involves superficial epidermis, <u>stratum granulosum layer</u>	IgG deposits on keratinocytes
Bullous pemphigoid	<u>Subepidermal non-acantholytic blisters</u> containing <u>lymphocytic and eosinophilic infiltrates</u>	Linear IgG ± C3 in epidermal BMZ
Epidermolysis bullosa acquisita	Subepidermal non-acantholytic blisters usually without leucocytic infiltrates. <u>Autoantigen vs collagen-VII +nt</u>	Linear IgG ± C3 in epidermal BMZ
Dermatitis herpétiformes	Neutrophilic microabscesses at dermal papillae, urticarial base	Granular IgA deposits in dermal papillae

SCALING DERMATOSIS

Photograph : Psoriasis

Feature	Psoriasis	Lichen planus
Type of d/s	Chronic inflammatory	<u>Self-limiting papulo-squamous d/s</u>
Lesions.	Well defined, scaly, red plaques on extensor surface	B/L symmetrical Flat-topped, <u>violaceous papules on flexor surface</u> (forearm, wrist / ankle) [Remember-5'p' Pruritic, Purpule, Polygonal, Plain top Papule]
Mucosa	Spared	+ White streaks with lacy network in oral mucosa
Flexural involvement	Seen in inverse psoriasis	+
Pruritus	Usually not	
A/w	<u>HLA-CW6 (Psoriasis)</u> HLA B ₂₇ , B ₁₆ , B ₁₇ , B ₁₃ (in arthropathy) Drug induced : chloroquine, β-blockers.	<u>HLA B-7, A-3, HCV</u> <u>T-cell infiltration in Dermis</u>
Nails	Thimble nails/pitting of nails, onycholysis Beau's lines	Pterygium formation (characteristic) Civatte bodies ⁺
Arthropathy	<u>DIP joints involved</u>	Rare
Other/f	Munro-microabscess Auspitz sign in active d/s, Woronoff's ring sign	<u>Wickham's striae</u> (white/grayish lines) <u>Scarring alopecia</u> is seen
T/t:	<u>DOC is PUVA</u> <u>Mtx for arthropathy</u>	Steroids, calamine lotion. <u>Lesions become hyperpigmented after t/t.</u> Mucosal --- Retinoids <u>AIDS, Pustular</u> --- Retinoids

→ Max-Joseph spaces, are artificial subepidermal clefts often seen in lichen ruber variants of Lichen planus



Photographs : Lichen planus with Kobner's phenomena

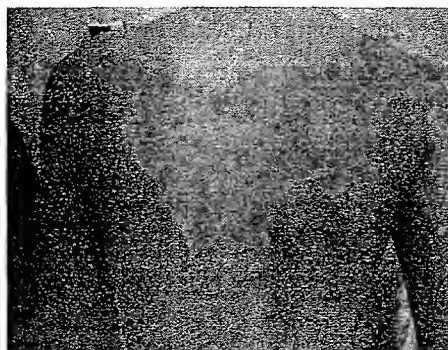
Psoriatic Arthropathy

- * Arthritis mutilans involves DIP joint
- ✓ Triad of pitting of nails (thimble nails) + ridging + onycholysis features of onychodystrophy
- * "Pencil in Cup" or opera glass appearance. Telescoping saucers shaped digit (dactylitis)
- * A/w seborrheic dermatitis, lichen planus, lichen chronicus, DM, hypocalcemia, malabsorption
- T/t : DOC is Methotrexate
Gockerman regime (UV-B + Coal tar) & Ingram regime (UV-B + tar + Dithranol)
- Topical steroid — In psoriasis of scalp face, flexures, and genitalia

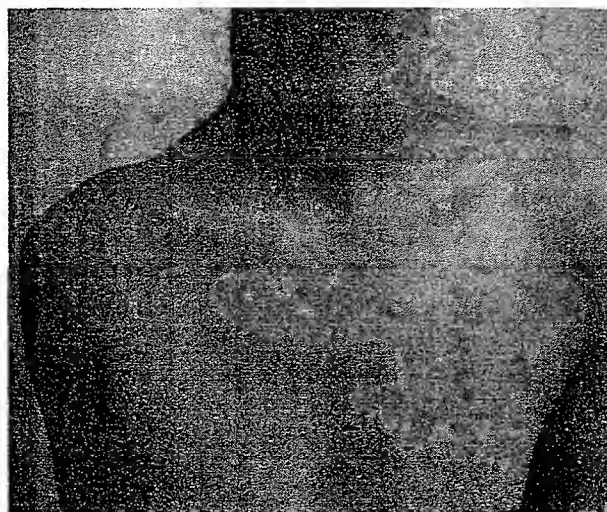
DISORDERS OF PIGMENTATION

Pityriasis Rosea

- Acute exanthematous papulosquamous eruption of unknown etiology seen in young females
- ✓ First feature is Herald patch + usually over trunk or upper arm, thigh.
- * Christmas tree / fir tree pattern of lesions (Secondary syphilis like lesions but spares palms and soles)
- ✓ Cigarette paper like scales.
- * A/w virus (HHV-7) One attack gives life long immunity.
- ✓ Mild SPONGIOSIS and focal exocytosis. Pruritus is -nt (or mild).
- Centre of lesion is depressed with marginal collarette of scales
- T/t- self limiting course.



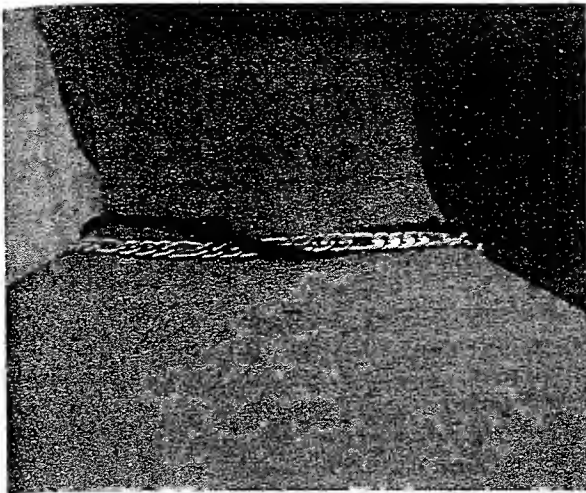
Photograph : Pityriasis rosea



Photograph : Inverted fir tree appearance

Pityriasis Versicolor / Tinea Versicolor

- M/c type of superficial mycoses caused by Malassezia furfur (Pityrosporum orbiculare).
- * Groups of light brown macules with furfuraceous scaling. Macules are hyperpigmented in whites / hypopigmented in dark skinned races. Seen over trunk, chest, back
- Yellow / golden fluorescence under wood's lamp.
- KOH microscopy shows characteristic "Spaghetti & Meatball" appearance or "Banana & grape appearance".
- ✓ Common in adults. May involve shoulder and trunk in children.
- ✓ Common in hot, humid, itchy climate.
- Central scarring (healing with scar formation) is seen in → Lupus vulgaris (diagnosed by biopsy)
- Central clearing of lesion is seen in → Tinea corporis (diagnosed by KOH smear)
- Central crusting is seen in Kalazar (Leishmaniasis), diagnosed by demonstration of LD bodies in BM.



Photograph : Pityriasis versicolor

Pityriasis Alba

- Non-specific dermatitis manifest as ill-defined hypopigmented round / oval macule with fine scaling on face of the child
- More common in winter.
- Disappears spontaneously by puberty.

Pityriasis lichenoides chronicus (PLC)

- Also k/ "Chronic guttate parapsoriasis/Chronic pityriasis lichenoides," "Dermatitis psoriasiformis nodularis," "Parapsoriasis chronica,"
- Uncommon, idiopathic acquired dermatosis, c/ by evolving groups of erythematous, scaly papules that may persist.
- In Pityriasis rubra pilaris isolated patches of normal skin are also seen.
- Herald patch is seen in - Pityriasis rosea

D/d of hypopigmented patch

Features	Age gp	Site	Characteristics
Recurrent scaly macule			
Pityriasis alba (simplex) Pityriasis versicolor	Children	Cheeks, face	
Non-scaly macule			
Indeterminate leprosy	Any	usually face	Anesthetic patch
Tuberous sclerosis	Young child		Ash leaf macule, shagreen patch
Vitiligo	-	Anywhere in the body	Sharply defined non-pigmented patch

Disorders of Pigmentation

Hyperpigmentation	Hypopigmentation
Addison's d/s	Vitiligo, piebaldism
Nelson syndrome	Nevus anemicus
Hyperthyroidism	Nevus depigmentosus
Cushing syndrome	Pityriasis
Ectopic ACTH Syndrome	Scleroderma
Freckles (Ephelids)	Sarcoidosis

* Nevus ota, ito, mangolian spots, cafe au lait spots are causes of local hypopigmentation!

Hypomelanotic lesions

Asymmetrical or U/L

Nevus achromicus	Single hypopigmented patch on thigh at birth + erythema response
Nevus anemicus	Same as above but <u>no</u> erythema response (pale lesion)
Albinism	Congenital (AR) d/s Complete absence of melanin Diffuse response

Symmetrical & Central

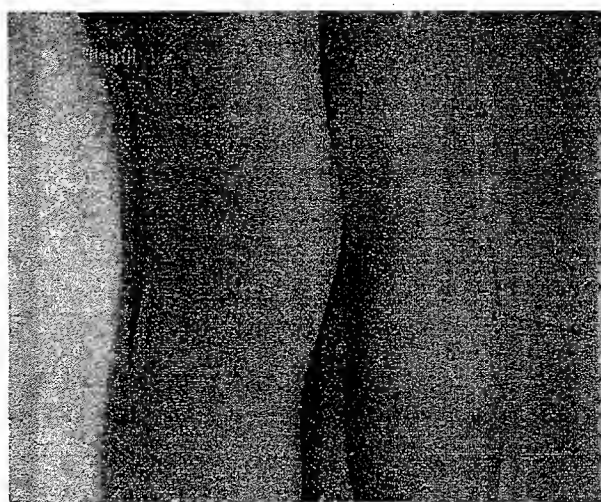
Piebaldism	Congenital (AD), Depigmented / hypopigmented patches of skin + <u>white forelock of hair</u>
Vitiligo	Acquired patchy depigmentation <u>a/w autoimmune d/s</u>

* ↑ incidence of vitiligo is found in DM, nutritional deficiency

DERMATITIS/ ECZEMA

ATOPIC DERMATITIS

- Family history of asthma / hay fever
- Flexural skin sites especially antecubital & popliteal fossa are involved.
- Pruritus is hallmark. Lichenoid lesions (common in infants).
- Perioral pallor, Dennie's line & Monk's crawl.
- Secondary infection is common with staph. aureus.
- T/t - Topical Glucocorticoids.



Photographs: Atopic dermatitis

CONTACT DERMATITIS

- * Also k/as acute contact dermatitis (ACD)
- Inflammatory process d/to exogenous agents.
- M/c presentation : hand eczema (which is related to occupational exposure of metals (nickel), drug (neomycin), airborne (Congress grass) & detergents (m/c cause of ACD in Indian females)
- M/c cause of air borne contact dermatitis in India : ACD d/to plant *Parthenium* (Congress grass).
- * Type 4 / Delayed type of HS reaction (mediated by memory T-cell in skin).
- * T/t : Topical potent glucocorticoids (esp. fluorinated)
- * D/g : Patch test (for Allergic CD). Scratch test with latex/RAST (for irritant CD / Hand eczema).
- Nummular eczema (discoid dermatitis) is circular / oval coin like pruritic lesions over trunk/ extensor surface of limbs in middle age males (M>F).
- Asteotic xerotic eczema (Winter itch) is inflammatory dermatitis with fine cracks. Seen in summer and involves lower legs in elderly.

Seborrheic Dermatitis

- Seborrhea is genetically determined factor.
- * A/w Parkinsonism, CVA, epilepsy, HIV, manic depression, cushing syndrome & some virilizing syndromes in female, breast cancer.
- * Greasy scale
- * "Cradle cap"

Ecchyma Gangrenosum:

- Edematous papules change into central purpura (palpable).
- * MC organism : *Pseudomonas aeruginosa*

Pyoderma Gangrenosum:

- * Generalized cutaneous ulcers. Ulcer begins as pustule → progress up to 20 cm. It has undermined bluish edge, peripheral erythematous halo
- Seen on lower legs but may present on site of trauma (pathergy test +)
- * A/w UC > CD, chronic active hepatitis, RA, PV, MM, AML, CML.
- * Diagnosis is made clinically (Morphology of lesions)

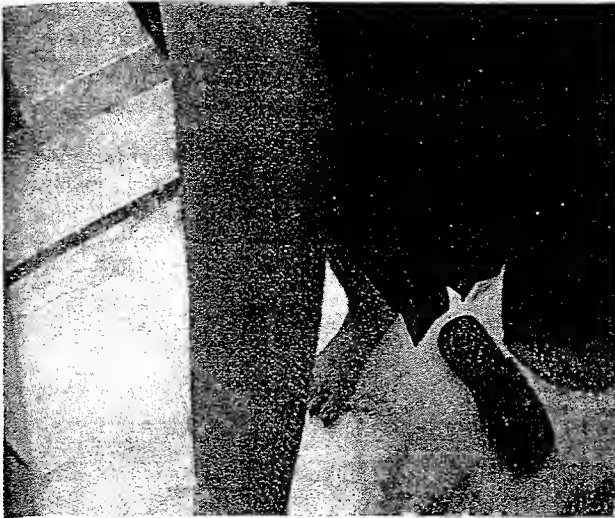
ERYTHEMA

Erythema Multiforme

- * Acute self limiting d/s of skin / mucous membrane.
- Characterized by target lesions (Bull's eye lesions or iris lesions). Lesions are vesicobullous, found at dermo-epidermal junction. Seen over face & upper limbs.
- Causes : HSV (m/c cause), drugs like sulfonamides (m/c drug), penicillin, phenytoin, phenylbutazone etc.

Erythema Nodosum

- * Panniculitis char/by crops of tender subcutaneous nodules d/to hypersensitivity.
- Lesions seen on anterior surface of legs/shin of tibia, forearm
- Causes,
Infections: streptococcal infection, TB, Leprosy (LL).
Drugs: OCP use, sulfonamides, Pn etc.
Sarcoidosis, Behcet's d/s, enteropathies, brucellosis, SLE, Pregnancy
- * Arthralgia is found in 50%



Photograph: Erythema nodosum

Other imp. erythemas

- ◉ E~ toxicum ---- Seen in normal neonates
- ◉ E~ infectiosum ---- 5th d/s by parvo virus B-19
- ◉ E~ marginatum ---- Rheumatic fever
- ◉ E~ annulare → Seen in (DM) over trunk
- ◉ E~ migrans chronicum ---- Seen in LYME DISEASE
- ◉ E~ gyratum repens ---- In malignancy
- ◉ E~ streptogenes → In Pityriasis alba
- ◉ E~ pernio ---- In chilblains

Ecchyma

- ◉ Deep infection of skin d/to GpA streptococci which involves extra follicular portion (i.e. hair follicles spared).
- ◉ M/c site buttocks, thighs & legs.

Erysipelas

- ◉ Inflammation of lymphatics of skin caused by streptococcus.

Erythrasma

- ◉ Chronic superficial infection of skin with mild erythematous patches in axillae, groins, toes webs.
- ◉ Caused by Corynebacterium minutissimum (produces porphyrins → coral red fluorescence on wood lamp).
- ◉ TOC: Oral erythromycin.

Urticaria Pigmentosa

- * Development of wheel on gentle stroking of a pigmented macule (Darier's sign).
- ◉ D/s of mast cells: systemic mastocytosis leads to → severe itching.
- ◉ (AD) inheritance in some cases (familial).
- * Recurrent diarrhea, reddish brown macule on torso / extremities.

D/d of Viral Exanthems

✓ Urticaria is 2nd most frequent type of cutaneous reactions to drugs.

- ◉ FDE (Fixed Drug eruptions) --

(One or more sharply demarcated) erythematous lesions, leading to blister. Hyperpigmentation results after resolution of acute inflammation. A/w phenothalein, sulfonamides, cyclines, dipyrone, NSAIDs, barbiturates.

- ◉ SJS (Steven Johnson Syndrome) --

Characterised by blisters & epidermal detachment.

A/w sulfonamides, nevirapine, allopurinol, lamotrigine, aromatic anticonvulsants, okicam NSAIDs...

Parapsoriasis

- ✓ Can progress to cutaneous T-cell lymphoma after latency of ~40 years.
- ✓ Small plaques are seen on trunks and large plaques on girdle area.

DERMATOPHYTOSIS

TINEA /RINGWORM

Dermatophytosis is a chronic fungal infection of skin, hairs or nails. It is also k/as "ringworm or tinea".

Tinea capitis

Infection of scalp caused by trichophyton tonsurans or microsporum canis. It can cause non-inflammatory infection with mild scale and hair loss or It may causes inflammatory boggy swelling (k/as kerion) with easily pluckable hairs Kerion is diagnosed by KOH smear. Occipital LN are enlarged ✓

Tinea corporis

Infection of glabrous or non-hairy skin of the body caused by microsporum, trichophyton.

Tinea cruris

Infection of groin thigh, perineum, perianal area (ringworm of groin/jock itch), caused by E. floccosum, T. rubrum and T. mentagrophytes. Adult males are affected commonly

Tinea pedis

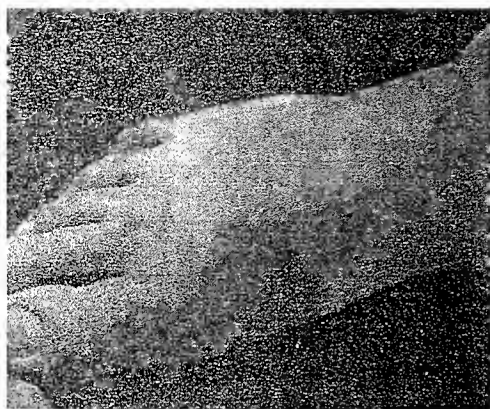
Infection of feet (athlete foot) caused by T. rubrum

Tinea unguum

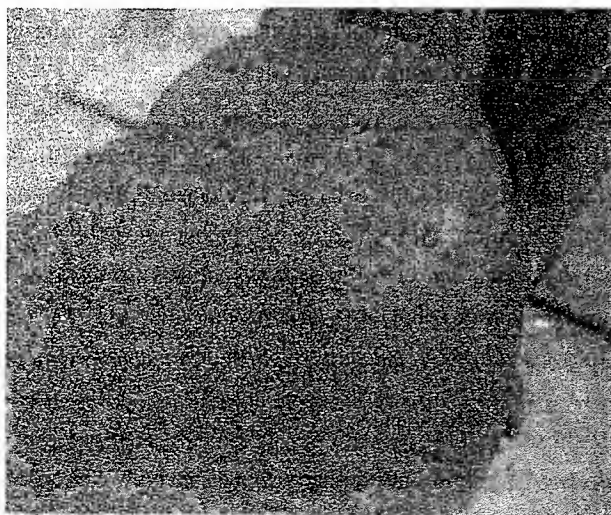
- ✓ Toe nail is mainly involved, involves soft keratin of nail bed & later nail plate (hard keratin)



Photograph: *Tinea unguis*



Photograph: *Tinea pedis*



Photograph: *Tinea capitis*

REMEMBER

Epidermophyton involves --- Skin + nail

Microsporum involves --- Head + skin

Trichophyton involves ---- Head + skin + nails

- Pediculosis is common infestation of children caused by blood sucking lice. They are named as per their habitat:

Habitat	D/s	Caused by	Cl/f, T/t
Scalp	Pediculosis corporis	Pediculosis <u>capitis</u> (head lice/nit)	1% GBHC lotion
Eyelashes	Pediculosis <u>palpebrarum</u>	Phthiriasis/ pediculosis pubis	apply vaseline
✓ Body	Pediculosis corporis	Pediculosis humanus (<u>body lice</u>)	"Vagabond d/s" is a variant
Pubic area	Pediculosis pubis	P. pubis	Bluish black pigmentation k/as ' <u>maculae caeruleae</u> '

- P. humanus should be searched in the clothing rather than in body.
- Close contacts with the infested transmits the d/s.
- ✓ Main t/t --- disinfection of clothes (essential in P.corporis).
All family members are to be treated simultaneously.

Imp Lines

- Dennie's line --- Extra fold of skin beneath lower lid (Seen in atopic dermatitis)
- ✓ Pistia line --- In Scarlet fever
- Beau's line --- Deep transverse groove in nail (Seen in psoriatic arthropathy)

Different ITCH

- * Winter itch -- Asteotic eczema / xerotic eczema
- Swimmer's itch -- Bilharziasis / Schistosomiasis
- Dhobi's / Jock itch -- Tinea cruris
- * Ground itch -- Nematode Larvae
- Barber's itch -- Sycoses barbae
- ✓ Itch mite -- Acarus scabei (which transmits Scabies)

SCABIES

- Caused by mite '*Sarcoptes scabei*'.
- * Cl/f- itching (m/c complaint), vesicles over anterior wrist, interdigital webs
- H/o disease in other family members
- ✓ Palms, soles & scrotum may be involved in infants (nodular scabies)
- * Burrows are pathognomonic which are found in stratum corneum. Commonest sites of burrows i.e. in the horny layer of the epidermis e.g. fingers, interdigital webs, palms,

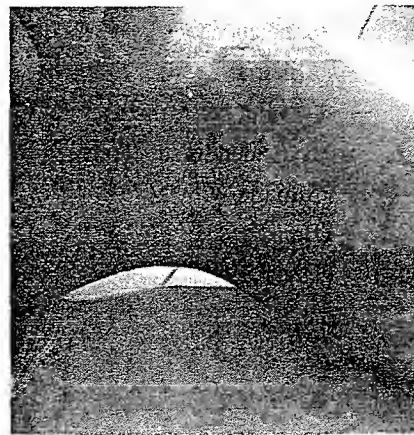
wrists, points of elbow, anterior axillary folds, nipples, abdomen genitalia, legs and feet. (Neck and face are usually not involved except in children).

- Fine pin head sized follicular papules. (Papulopustules or erythematous bases) are commonly seen.
- * DOC is permethrin Gamma BHC is also useful (NO role of antibiotics) **
- Scabies incognito : Scabies wrongly treated with steroids
- Norwegian scabies : Most severe form seen in old, malnourished, immunosuppressed person. Also seen in patient of Down syndrome. Usually resistant to t/t



- Scrofuloderma is c/by focus of infection in deep tissues (LN/bone, joint) and formation of discharging sinuses in skin. Healing with cord like scars.

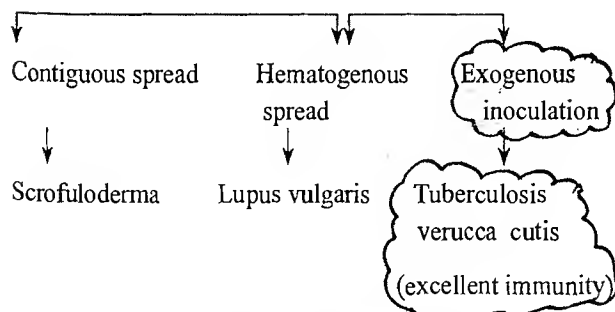
- TB cutis orificialis is c/by autoinfection around orifices like muco-cutaneous junction. Nodular lesions around lips/mouth/anus. No tendency to heal.



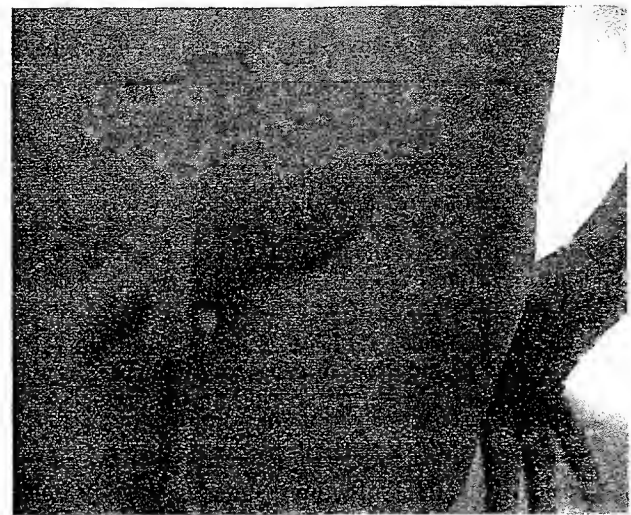
Photograph: *Lupus vulgaris*

TB-Skin

- Caused by *Mycobacterium tuberculosis bovis* and under some conditions by *BCG*.
 - Primary TB : TB chancre, usually on extremities.
 - Re-infection TB : After a latent period re-infection occur & depending upon immunity level skin necrosis may occur.
- 3 FORMS ARE SEEN -



- Lupus vulgaris is m/c and mild form. Face, nose, buttocks are affected. No bacilli / focus is found
- TB verruca cutis is moderate (warty) form d/to external inoculation. Found in persons handling tuberculosis tissue i.e. it is an occupational hazard.



Photograph: *Scrofuloderma*

TUBERCULIDS

Group of eruptions usually symmetrically distributed as a result of infection from internal focus. Two types are seen.

- Papulonecrotic tuberculids is m/c form c/by chronic recurrent, symmetrical necrotic eruptions of papules.
- Lichen scrofulosorum is c/by presence of non-caseating granuloma caseation around hair follicles and sweat ducts.

DISORDERS OF SKIN GLANDS

- Sebum is composed of mixture of lipid+ cholesterol+
- Sebum is composed of mixture of lipid+ cholesterol+ epidermis+TG - squalene, oils/wax. Secretion of holocrine sebaceous glands.

* Pilosebaceous gland ---- Acne vulgaris, for dyce spots of neonate

- Sweat gland ---- Miliaria
- Apocrine gland ---- Fox Fordyce's disease
Hydradenitis suppurativa

- Sweat gland ---- Miliaria

* Hair root ---- Boil

- Diseases of eccrine sweat glands

-- Hyperhydrosis

-- Anhidrosis

-- Miliaria

✓ Multiple sebaceous tumours are seen in Mui-Torr syndrome.

- Hydradenitis suppurativa (acne inversa) is a d/s of ducts of apocrine glands or sometimes sebaceous glands.

→ Fox Fordyce disease involves axilla and pubis

→ Fordyce spots are ectopic sebaceous glands in neonates.

Spots

- Fordyce spots are ectopic sebaceous glands, not a/w erythematous halo, found in healthy neonates.

* Forchheimer's spots are palatal petechiae found in German measles (Rubella), infectious mononucleosis, scarlet fever.

* Koplik's spots are 1-2 mm white/blue lesions, pathognomic for Measles.

Acne Vulgaris

- Self limiting disorder of teenagers and young adults
- D/to obstruction of sebaceous glands leading to retention of sebum
- Multiple papulopustular erythematous lesions over face and neck

✓ Earliest lesions and hallmark of the d/s are comedones usually over face (forehead, nose cheeks) shoulder, back and upper chest are other locations.

* Infected with propionobacterium acne or a yeast pityrosporum orbiculare

DOC for

* ~~IRRE~~ → CYPROTERONE Acetate

✓ Nodulocystic acne is --- topical retinoids (isotretinoin) which are comedolytic.

✓ For inflammatory acne --- Minocycline

✓ M/c ad/e of tretinoin is skin rash Other ad/e are hypertriglyceridemia, teratogenicity

- Retinoic acid (Retinoids) are DOC in Acne vulgaris, comedonal acne, nodulocystic acne, pustular acne. M/c side effects are dryness of skin, chapped lips, & xerosis (mucocutaneous/ocular) mouth.

* Rhinophyma is glandular form of rosacea.

* If a teenager girl with moderate acne complaints of moderate acne a/w irregular menses, drug of choice is: Cyproterone acetate, administered in a reverse sequential regimen along with ethinyl estradiol. This schedule allows regular menstrual bleeding, and is effective in t/t of severe acne and hirsutism. **

DISORDERS OF HAIR

Phases of hair growth

Anagen --- Growing phase (90% of hair are in this phase)

Catagen --- Involutionary

Telogen --- Resting /dying phase

Alopecia Areata (Non-cicatricial alopecia)

- Cause is unknown but is believed to be immunological. (A/w infiltration of lymphocyte in germinal zone of hair follicles)

- May be a/w autoimmune disorders - Hashimoto's thyroiditis, pernicious anemia, Addison's disease and vitiligo.

Also seen in-- Psoriasis, SLE, tenia capitis, secondary syphilis

- Typically, there are patches that are perfectly smooth and without scarring.

- Exclamation marks (!) are seen

- Involvement may extend to loss of all hair from scalp (Alopecia totalis) or all scalp and body hair (Alopecia universalis)

- T/t : Intralesional steroids, minoxidil

✓ Androgenetic alopecia is the m/c form of alopecia, genetic predisposition is common.

→ Telogen effluvium --is transitory ↑ in the no. of hairs in the telogen (resting) phase of hair growth. Seen d/to stress/ hormonal change (e.g. post partum). Club hairs are seen

- **Chrysisis** : Blue grey pigmentation of tissue & hair. Seen after parenteral administration of gold salts.

Scarring /cicatricial alopecia (Pseudo pelade)

- Is irreversible and permanent.
- Causes are-- chemical, physical trauma, lichen planus (HZV) Chronic DLE, Scleroderma, ionizing radiation and severe bacterial, fungal infections.
- * Pseudo pelade of Brocq is (rare) type of scarring alopecia which affects "middle aged people".

Chemical peeling is done by

- TCA (Tri-chloroacetic acid).
- Salicylic acid
- Pyruvic acid
- * "Kojic acid"

DISORDERS OF NAILS

- Tinea unguis involvement is seen in nail plate
- Koenen's periungual fibroma is seen in --- tuberous sclerosis
- Mee's line --- Arsenic poisoning
- **Half and half nail sign** is seen in --- Uremia
- Longitudinal ridges --- Median canaliform Heller's dystrophy.
- Koilonychia is seen in IDA (iron deficiency anemia), Plummer Vinson's syndrome.
- Pachyonychia is a "thickened plate like nails". Seen in hyperparathyroidism, vit D therapy or may be congenital.
- * Pterygium, anychia, pitting is seen in lichen planus
- Onychylosis, ridging, pitting, oil drop nail, thimble nails are seen in psoriasis.
- **Trachyonychia** is nail dystrophy.

Cafe-au-lait spots are seen in

- Neurofibromatosis (Von Recklinghausen's d/s)
- Albright's syndrome & Fibrous dysplasia
- * Watson's syndrome
- * LEOPARD Syndrome
- * Fanconi's anemia

Leonine facies are seen in

- LL-Leprosy
- Paget's disease of bone
- Fibrous dysplasia
- Hyperphosphatemia

PURPURA

Palpable purpura seen in -

1. Vasculitis

- * Leukocytoclastic vasculitis - m/c cause
 - **HSP**
 - Mixed essential cryoglobulinemia
 - CTD, Lupus vasculitis, PAN, hepatitis C antibiotics etc.

2. Infections

- * Ecthyma gangrenosum
- * Acute meningococemia, Gonococemia
- * RMSF

[mnemonic to remember PARLE-G Meetha Hai]

- * Non-palpable purpura is d/to ITP, platelet dysfunction, DIC/ TTP, cholesterol/ fat emboli
- * Pinch purpura (purpura d/to ↑ed capillary fragility) is seen - Primary systemic amyloidosis, EDS, scurvy.
- HSP is a/w palpable purpura without thrombocytopenia.
- * Hypersensitivity vasculitis or cutaneous leukocytoclastic angitis is seen in --- Post capillary venules

SYPHILIS

- * M/c route of transmission: sexual Also transmitted by BT, transplacental.
- Direct microscopy is done for 1^o and 2^o syphilis. Much useful in 1^o syphilis. Dark ground microscopy & silver staining are used. (Gram staining is NEVER done)

Primary S-

- Lesion is k/as "primary chancre (hard sore)": Chancre is indurated, single, painless, indolent, exudes clear /serous fluid on manipulation. It is present at the site of coital trauma.
- * LN are multiple, discrete, non-tender, rubbery, (B/L)
- Usual order of conversion: - FTA → VDRL → TPHA (earliest test to become +ve is FTA-ABS)
- * VDRL becomes (+ve) in 1-2 weeks after appearance of ulcer
- * **Regional Lymphadenopathy** (Shotty enlargement of LN) develops usually after 1 week of chancre.

Secondary S-

- Develops 6-8 weeks after appearance of primary chancre
- Skin lesions are in form of diffuse symmetrical dull red maculopapular rashes.
- * Rashes over palms & soles are characteristic. (but no bullae).
- Generalized non-tender lymphadenopathy.
- Mucous lesions are also present. Soft sore, snail tract ulcer and perianal condyloma lata are seen.
- Rarely hepatosplenomegaly, anterior uveitis, bone/joint pains, nephrotic syndrome, *pneumonia alba* are seen.
- Moth-eaten Alopecia.
- ✓ Highly infectious stage and all serological tests are 100% sensitive.
- Treponema may be found in aqueous humor

Tertiary / Late S-

- Develops 3-10 years after primary lesion usually following untreated secondary syphilis.
- Typical lesion is "gumma"
- Gummas tend to heal at centre leaving "tissue paper scar"
- Mucosal gummas are painless, *punched out ulcers* (bony gumma in tibia & cranial bones).

NEUROSYPHILIS: Major clinical categories

Meningeal S-	<ul style="list-style-type: none"> Onset < 1 yr of infection * Involves brain/ Spinal cord Headache, N/v Neck stiffness CN involvement * Seizures * Uveitis/iritis
Meningo-vascular S-	<ul style="list-style-type: none"> After <u>5-10 yrs</u> of infection. * Diffuse inflammation of pia/ arachnoid M/c presentation: stroke d/ to MCA involvement ✓ <u>Subacute encephalitic Prodrome</u>
General paresis	<ul style="list-style-type: none"> After <u>20 years</u> of infection * Late parenchymal damage, <u>personality changes</u> Affects--- <ul style="list-style-type: none"> - Reflexes (hyperactive) - Eye (ARP) ✓ <u>Sensorium (illusion/delusion)</u> ✓ <u>Intellect</u> * Charcot's jt
Tabes dorsalis	<ul style="list-style-type: none"> After <u>25-30 years</u> of infection * Demyelination of posterior column Ataxic, wide based gait Areflexia Loss of position deep pain, temp. sensation * Optic atrophy m/b seen * Argyll Robertson's Pupil (ARP)

SYPHILIS: STAGES

Stage	C/F	T/t
Prenatal	Cross Langan's layer after 4 months,	ACPG
CS:	chorioamnionitis, necrotizing funisitis	
Placental		
Prenatal	Hydrops, IUGR,	ACPG
CS: Fetal	Prematurity, stillbirth	
Postnatal	Manifest in <2 yr of life	ACPG
CS: Early	Highly infectious (resembles 2° S-)	
	* M/c early/f - Osteochondritis/Osteo-osteitis, dactylitis+, epiphysitis+	
	✓ Snuffles (earliest symptoms)	
	Salt & pepper fundus chorioretinitis,	
	Saddle nose	
	Bullae+ /Pemphigus like vesicles	
	Hepatitis,	
	* Parrot's pseudoparalysis,	
	Rhagdes (Scars at ∠ of mouth),	
	✓ Wimberger sign +ve	
Postnatal	Seen after 2-3 years of age	
CS: Late	Deafness	ACPG
	✓ B/L effusions of knee joints (<u>Clutton's Jt.</u>)	
	Interstitial keratitis	
	* Perfora ⁿ of palate, NS destruction	
	Sabre shins/ tibia	
	✓ <u>Mulberry / Moon's molars</u>	
	Bony mass in skull (<u>Parrot's nodes</u>)	
	Neurosyphilis,	
	* <u>Higoumenaki's sign</u>	
1°	Primary chancre, <u>Follman's balanitis</u> , <u>chancre re'dux</u> , 'dory flop' sign,	BPG
2°	Condyloma lata, <u>Biette's collarate</u> , 'frambesiform syphilid', leucoderma colli (collar of venus), leus maligna, moth eaten alopecia, mucous patches, Ollendorff's sign, split papule, nephrotic syndrome, granulomatous iritis, retrobulbar ON, other c/c	BPG
Latent	Asymptomatic	
3°	Gummas, <u>Pseudo-<u>chancre re'dux</u></u> , <u>b/L bursitis of Verneuil</u> , <u>Charcot's joints</u> , Aortitis, stenosis of coronary ostia, <u>Aortic aneurysm involving ascending aorta</u>	ACPG

T/t of syphilis

1. CNS syphilis & congenital syphilis → ACPG (Aqueous crystalline Pen G) or Procain penicillin G.
2. 1°, 2° & Early latent syphilis → BPG (Benzathine Penicillin G) single i/m dose of 2.4 million U.
3. Late latent syphilis → Benzathine Penicillin G i/m 2.4 million U weekly x 3 week.

→ Characteristic triad of congenital syphilis is k/a/s -- Hutchinson's triad (deafness + interstitial keratitis + Hutchinson's teeth)

→ Lesions of congenital syphilis develop only after the 4th month of gestation.

Tests for Syphilis

- For screening → VDRL test is used.
- Tests used now a days → TPPA (Treponema particle agglutination).
- Response to t/t is assessed by --RPR test or quantitative VDRL.
- Diagnosis of congenital syphilis is established by --- **IgM-FTA ABS test** in neonatal serum.
- Most sensitive test --- FTA - ABS
- Most specific test --- TPI (but it is costly and available in limited centres) > FTA - ABS. Once +ve always +ve.
- * Negative TPHA virtually excludes the diagnosis of syphilis.
- ✓ Treponemal tests. TPI, FTA-ABS, IgM-FTA-ABS. These test can not differentiate b/w past/recent infection.
- Non treponemal tests : "Cardiolipin Ag based". VDRL, Wasserman, Kahn's. These tests are cheap, indicate ongoing d/s, c/b used for prognosis, become -ve on t/t. false +ve reactions are seen in pregnancy, SLE, RA, malaria, leprosy.
- Interpretation.

→ Incubation period of syphilis is 10 to 90 days (median i.p. is 21 days)

* In T/t of CNS syphilis and congenital syphilis --- Pen G (Procaine Pen). Rest all syphilis Benzathine Pen

* Reagin antibody appears "after 7-10 days of appearance of primary chancre or 3-5 wks after infection".

→ Chancre redux is seen in primary syphilis.

→ Pseudo-chancr redux is "recurrence of syphilitic chancre at the site of previous chancre". Seen in tertiary (late) syphilis.

Non-treponemal test	Treponemal test	Interpretation
+	+	Active ongoing syphilis
+	-	False +ve non-treponemal test (SLE, RA, preg, malaria)
-	+	Past treated infection

	VDRL/RPR	FTA-ABS	TPHA
1° Syphilis	70-80%	<u>80-100%</u>	65-85%
2° syphilis	100%	100%	100%
Latent syphilis	60-70%	<u>95-100%</u>	95-100%
Nonvenereal treponema	+ve	+ve	+ve
✓ Lyme Disease	<u>-ve</u> ***	+ve	
✓ Leprosy/Malaria	<u>+ve (false)</u>	-ve	-ve

Syndromic Management of STD's

Applied to following d/s :

- Urethral discharge in absence of lab support.
for gonorrhoea, chlamydia
- * Genital ulcer in absence of lab support.
for syphilis, herpes & chancroid
- Inguinal bubo in absence of lab support.
for syphilis, LGV
- Vaginal discharge in absence of lab support but P/S examination is possible.
for trichomoniasis, bacterial vaginosis, candidiasis, , gonorrhoea, chlamydia

D/D OF GENITAL ULCERS

	Syphilitic chancre (Hard sore)	Chancroid (Soft sore)	Herpes	LGV (Lymphogranuloma venereum/ inguinale)	GI (Donovanosis)
Primary Lesion	<u>Painless, indurated</u> usually single ulcer with punched out edges	<u>Painful, non-indurated</u> usually multiple ulcers that begin as small tender papules, soft base (soft sore)	Vesicles, painful lesions	Primary genital lesion (herpetiform vesicle/ ulcer) is usually missed by patient → <u>f/b multilocular</u> <u>regional LN usually</u> <u>inguinal syndrome</u>	✓ <u>Button like papule with bright</u> <u>ulcer which bleeds on touch</u>
Ulcer	Single, large (5-15 mm) firm indurated	<u>Multiple, excavated</u> <u>ulcers which bleed on</u> <u>touch, very painful</u>	Multiple, small, 1-2 mm	Usually transient single 2-10 mm, non-vascular	<u>Variables red velvety firm</u>
LN	Firm, non-tender B/L	Loculated usually u/L	Firm, tender, usually B/L	Loculated, tender, usually u/L, suppurative	Pseudo bubo (No lymphadenopathy) Apparent LN↑
Etiology	<i>T. Pallidum</i>	<u><i>M. ducreyi</i> (school of fish appearance),</u> ✓ <u><i>Herpes virus hominis</i></u> ✓ <u><i>N. gonorrhoeae</i></u> , ✓ <u><i>Staph. albus</i></u>		<i>Chlamydia</i> <i>trachomatis</i> (McCoy cell culture +ve)	<i>Calymmatobacter donovani</i> (<i>Donovania granulomatis</i>)
Clf	Lesions at the site of coital trauma are characteristic	* <u>Ito test +ve</u> * Inguinal bubo's +, shotty LN (ulcerate with single opening) * <u>Prepuceal margin</u> <u>is m/c site</u>	Distribution along dermatome <u>c/b seen in zoster</u>	* Biopsy shows crypt abscess, Granulomas, giant cells (resembling Crohn's ds) ✓ Inguinal <u>bubo</u> with Multiple openings (Sign of groove) ✓ Genital elephantiasis (<i>esthiomene</i>) ✓ Anorectal syndrome ✓ D/g by : <u>Frei's test</u>	* Donovan bodies + Mikulicz cells + <u>satellite lesions</u> * Spread by auto inoculation & results in diffuse intra-dermal/sub-cut swelling (<u>pseudobubo</u>)
DOC	BPG 2.4 million U single i.m. dose	* Single dose of Azithromycin (or i/m ceftriaxone) * <u>Bubo should be</u> <u>aspirated</u> (<u>never incise it</u>)		* DOC : Doxy or erythro for 2 weeks	* DOC : Azithro

Non-veneral/ Endemic Treponematoses

- Yaws, Pinta & endemic syphilis (Bejel) are 3 important non-veneral trypanomatoses
- * VDRL, FTABS & TPHA all are positive.
- Transplacental, congenital transmission does NOT occur in yaws.
- TOC is BPG

D/s	Also k/as	Caused by	T/t
Bejel	Endemic syphilis	<i>T. pallidum</i> like organism	BPG 0.6 mega U (<10 yr), 1.2 mega U (>10 yr)
Pinta		<i>T. carateum</i>	BPG 0.6 mega U (<10 yr), 1.2 mega U (>10 yr)
Yaws	Pian, bubas, framboesia	<i>T. pertenue</i>	-

LEPROSY

Spectrum of d/s

Type	C/F	Remark
Pure neuritic	Slit smear - ve, Painless trophic ulcers+	-
LL	Subepidermal free zone, Lucio phenomena, Lazarine leprosy reaction,	Globi+++
TT	Single skin lesion, M/c type in India & Africa	CMI +++
BB	Inverted saucer lesions (BB > BL)	Most unstable form of leprosy
BT	Satellite lesions, M/c type in south east Asia	

* Satellite lesions are seen in - BT

- "Inverted sucer shaped ulcers" are seen in - BB (Borderline leprosy).
- * Globi are macrophages filled with lepra bacilli (AFB+) present in dermis.
- Virchow cell is diagnostic (found in lepromatous leprosy).
- Subepidermal zone is affected in tuberculoid leprosy while supra-epidermal zone in LL.
- TT
Lesion is well defined, macular, anesthetic lesion, usually

non-infectious (B⁻).

Lepromin test +ve, high CMI, highly resistant form.

LL

CMI depressed, very high bacillary load (B⁺⁺) (leonine facies) are seen

Lepromin test -ve

Lucio phenomena is seen in --- LL (Lazarine leprosy + is a form of LL).

* Pure neuritic leprosy --- Nerve involvement without any skin lesions, painless trophic ulcers +

- 1st sensation to be lost is temperature and pain.
- Part of nerve to be involved first is schwann cell.
- Nerves commonly involved --- Ulnar (most common), posterior tibial, great auricular, + lateral popliteal
- Radial nerve is involved last but if it is involved complications are more serious.

Reactions in Leprosy:

	Type-1 (Reversal reaction)	Type-2 (ENL)
1. Seen in	Borderline leprosy (BL)	Multibacillary leprosy (in LL, some BL)
2. Cause	Sudden increase in effective CMI in response to rapid killing of bacilli	D/to activation of T-helper cells polar LL form (in some BL patient.)
3. HS reaction	Type IV	Arthus reaction (type-3 HS reaction)
4. Cl/f and c/c	Acute tenderness and swelling at the site of skin/nerve lesions Acute neuritis can lead to irreversible nerve injury (Foot drop / Wrist drop)	Tender inflamed subcutaneous nodules
5. T/t	In mild cases NSAIDS In severe cases <u>high dose glucocorticoids</u> are DOC. No role of thalidomide in type 1 reac ⁿ	Glucocorticoids are DOC. <u>Clofazimine/ aspirin</u> is also effective

T/t of Type 2 lepra reaction or ENL

- If ENL is mild --- antipyretics (paracetamol)
- In cases of many skin lesions, fever, malaise --- Brief course (1-2 weeks) of glucocorticoids are often effective.
- * If despite two courses of steroids, ENL persists and is recurring → t/t with thalidomide should be initiated.
- * Clofazimine in high doses & Chloroquine also have some efficacy against ENL.

→ T/t of single lesion leprosy is ROM regimen = single dose of Rmp + Ofloxacin + Minocycline.

→ T/t of acute neuritis is --- prednisolone.

→ T/t of nerve abscess --- I & D

SOME IMP. NEGATIVE POINTS

- Pruritus is NOT seen in --- Pemphigus
- NOT seen in secondary syphilis --- Bullae or vesicobullous lesion.
- NOT a topically used antifungal --- Griseofulvin
- Griseofulvin is NOT used in T/t of --- Tinea versicolor, candida
- Erythema nodosum is NOT seen in ---- Infective endocarditis, pancreatitis
- Nail involvement is NOT seen in --- DLE
- Drug NOT given in t/t of alopecia --- Testosterone
- Drug NOT used in t/t of acne --- Androgens
- Alopecia is NOT seen in --- Psoriasis
- NOT a primary cutaneous d/s --- Reiter's d/s
- Kobner phenomena is NOT seen in --- Condyloma acuminata
- Genital Ulcers are NOT seen in --- LGV
- Lymphadenopathy is NOT seen in --- G.I.
- Lesions NOT seen in Lepromatous Leprosy --- Vesicles
- NOT commonly used for chemical cauterization--- Phosphoric acid.
- NOT true about Yaws --- Heart and CNS is involved in later stages
- Transplacental transfer is NOT common in --- HBV/ ?herpes
- Tests which are NOT useful in monitoring response to therapy in syphilis --- FTA-ABS and agglutination tests
- False about lithium --- ?Psoriasis is exaggerated.
- NOT caused by UV rays --- Verrucus verruca (warts).

CLINICAL VIGNETTES

- ❑ A 11 year old girl presents with 2-3 hypopigmented patches over right side of face. Most likely cause of it is

[DNB MAMC' 2008]

- A. Vitiligo B. Tinea versicolor
C. Pityriasis versicolor D. Pityriasis alba

(Ans. D. Pityriasis alba)

- ❑ An 18-yr-old boy presented with asymptomatic, multiple, erythematous, annular lesions with a 'Collarets of scales' at the periphery of the lesions, which are present on trunk. Most probable diagnosis is? [AI'05, 12]

- (A) Pityriasis rosea
(B) Pityriasis versicolor
(C) Pityriasis rubra pilaris
(D) Pityriasis alba

(Ans. D. Pityriasis rosea)

Vitiligo --

There are symmetrical hypopigmented (or non-pigmented) b/L lesions which are well defined. Lips are also involved.

Pityriasis alba

There are 2-3 asymptomatic, ill defined b/L hypopigmented patches seen in children. Resolves spontaneously. No treatment is required.

Pityriasis versicolor

Also k/as **Tinea versicolor**. Fungal infection caused by *Pityrosporum orbiculare* (*Malsazia furfur*). Usually affects **adults**. There are multiple asymptomatic, well defined hypopigmented or hyperpigmented small macules with fine scaling. Usually involve dark skin of chest & neck but face is usually not involved.

- ❑ A 10 year old school girl has recurrent episodes of boils on the scalp. The boils subside with antibiotic therapy but recur after some time. The most likely cause of the recurrences is : [AIIMS may'07]

- A. Primary immunodeficiency syndrome
B. Juvenile diabetes mellitus
C. Pediculosis capitis
D. HIV infection.

(Ans: Juvenile DM)

Boils may recur in *diabetics* or predisposed individuals e.g. malnutrition, systemic steroids, obesity, lymphomas

- ❑ A 25 year old male had pigmented macules over the palm, sole and oral mucosa. He also had anemia and pain in abdomen. the most probable diagnosis is :

[AIIMS May'07]

- A. Albright's syndrome B. Cushing's syndrome
C. Peutz-Jegher' syndrome D. Incontinentia pigment.

(Ans: Peutz-Jegher' syndrome)

Clue to d/g

Albright syndromes

Age/sex — Females with precocious puberty

Location — Midline larger, more irregular

Characteristic — Localized café au lait spots

Peutz-Jeghers Syndrome

- Affects Adolescents and children mainly but may affect adults.
- Autosomal dominant
- Onset in early childhood/infancy with pigmented macules over lips, buccal mucosa (occasionally on palate, gums, tongue, vagina)
- Pigmented macules often fades from lips and skin during puberty and adulthood (but not from mucosa)
- Polyposis usually involves Jejunum and ileum but may involve stomach, duodenum, colon and rectum.
- Episodic abdominal pain, diarrhea, hemorrhage/ malena (leading to anemia) and intussusception are frequent complications.

Incontinentia Pigmenti (Bloch-Sulzberger disease)

- Present at birth or develop within few weeks of life
- Hyperpigmentation in form of macular whorls (characteristic) over trunk, reticulated patches, flecks linear streaks axilla and groin are commonly attached
- *Lesions begin to fade by early adolescence and almost invariably disappear by 16 yrs.*

Cushing Syndrome

- Occurs between 20-40 yrs. F : M = 3 : 1
- C1/f : Rounded/moon face, protuberant abdomen, central obesity, hirsutism, cubitus valgus, amenorrhea, pigmentation in form of abdominal striae, purplish tinge esp on abdominal wall.
- X-ray will show — Osteoporosis, vertebral collapse , painless multiple rib #

- Q A 6 month old infant presented with multiple papules and exudative lesions on the face, scalp, trunk and few vesicles on the palms and soles for 2 weeks. His mother had history of itchy lesions. The most likely diagnosis is :

- A. Scabies
- B. Infantile eczema.
- C. Infantile seborrhoeic dermatitis
- D. Impetigo contagiosa

(Ans: Scabies)

Points in favour of scabies are ---

- Family history present
- Infant have papules on face, palm and soles
- Lesion is itchy

- Q A 48 year old sports photographer has noticed a small nodule over the upper lip from four months. The nodule is pearly white with central necrosis, telangiectasia. The most likely diagnosis would be: AIIMS May '06]

- A. Basal cell carcinoma
- B. Squamous cell carcinoma
- C. Atypical melanoma
- D. Kaposi's sarcoma.

(Ans.: A. Atypical melanoma)

48 yr old sports photographer is at risk direct exposure to sunlight which is risk factor for BCC, SqCC and Atypical melanoma. *Now clue to d/g are*

- **BCC** usually presents as an ulcer over the face in a middle aged man. Ulcer is non tender, dry, slowly growing, non-mobile
- **Atypical melanoma** may occur as pearly white nodule with central necrosis, telangiectasia.

- Q A 23 yr old man presented with fever and nodules on the skin for 3 weeks. A skin biopsy reveals aggregates of foamy histiocytes and neutrophils in the dermis. The most likely diagnosis is [AIPGMEE' 2009,2011]

- A. Sweet syndrome
 - B. Erythema nodosum leprosum
 - C. Erythema elevatum diutinum
 - D. Rosai Dorfman disease
- (Ans. B. Erythema nodosum leprosum)

ENL

- Seen mostly with LL leprosy
- Sudden appearance of crops of pink coloured tender nodules or plaques all over the body.
- Histopathology shows foamy histiocytes and large no. of neutrophils in dermis.

Sweet syndrome

- Also k/as acute febrile neutrophilic dermatosis
- Distinctive skin lesions which are initially small but later enlarge. Lesions are tender.

- Cl/f: A/w moderate to high fever, pink eye/ conjunctivitis, aching joint pain, mouth ulcers, tiredness etc.

- ▢ Involvement of sweat glands, dermal appendages, and hair follicles, with epithelioid granuloma are found in
A. Miliary tuberculosis B. Lichen scrofulosorum
C. Papulonecrotic tuberculid D. Lupus vulgaris

[AIPGMEE '2009]

(Ans: B. Lichen scrofulosorum)

- Tuberculids are skin reactions that exhibit tuberculoid features histologically (e.g. granuloma) but do not contain detectable mycobacteria. It occurs in individuals with h/o TB.

1. M/c observed tuberculid is **papulonecrotic tuberculid** in which there is recurrent crops of b/l symmetrical, firm, sterile, dusky red papules are seen over dorsum of hands, extensor surface of limbs, and buttocks.

2. **Lichen scrofulosorum** is another form c/by asymptomatic grouped, pin head sized often follicular (hair follicles involved) papules which are pink/red in colour. There are lichenoid eruptions of minute papules in adolescents. Healing occurs without scarring.

- ▢ A 10 yr old boy comes with boggy swelling of scalp with multiple sinuses and easily pluckable hair. Lymph nodes in occipital region were enlarged. Which of these will help in diagnosing the cause.

[AIIMS Nov'09]

- A. Biopsy B. Culture
C. KOH slide D. Patch test

(Ans: KOH slide)

- ▢ 19 year old sexually active male had recurrent erythematous eruptions on the glans. In between the eruptions he had residual hyperpigmentation. What is the probable cause:

[AIIMS Nov'09]

- A. Genital aphthosis B. Fixed drug eruption
C. Herpes genitalis D. Candidal balanoposthitis

(Ans: Fixed drug eruptions)

- ▢ Young boy presented with multiple flaccid bullae on trunk and buccal mucosal lesions. Most likely finding would be.

[AIIMS Nov'09, Nov'11]

- A. Fish net IgG in epidermis
B. Linear IgA deposits in dermal papillae
C. Linear IgG
D. Granular IgA in reticular dermis

(Ans: Fish net IgG in epidermis)

Flaccid bullae on trunk and oral/buccal mucosa are seen

in pemphigus vulgaris. Fish net IgG in epidermis are diagnostic. See table given in the text.

- ▢ A primigravida develops scaly skin lesions, erythema with pus surrounding the lesion. Drug of choice is:

[AIPGMEE '10]

- A. Methotrexate B. UV-A + Psoralen
C. Corticosteroids D. Isotretinoin

(Ans: C. Corticosteroids)

Most likely d/g is **pustular psoriasis**. Pustular psoriasis may improve spontaneously in upto 50% of patients in pregnancy. Topical steroids c/b used for localised d/s. Stepwise approach is suggested. If unresponsive to steroids then calcipotriene → anthralin → tacrolimus → UVB → psoralenes + UVB → upto oral cyclosporine c/b used in stepwise fashion.

Use of methotrexate, isotretinoin, cyclosporine, tacrolimus is contraindicated in pregnancy.

- ▢ A farmer have single wart lesion on leg. Most likely lesion is ---

[AIIMS 2010]

- A. Tuberculosis verrucosa cutis
B. Verruca vulgaris
C. Mycetoma
D. Lichen planus hypertrophicus

(Ans: A. Tuberculosis verrucosa cutis)

TBVC is a common condition seen in farmers. The lesion is usually a single warty plaque with induration. Cleft and fissures of the lesion discharge pus and there is central scarring.

In contrast lesions of verruca vulgaris are usually multiple and can occur anywhere on the body.

- ▢ A 25 year old man with history of multiple, unprotected heterosexual contacts with commercial sex workers, presented with multiple, non-indurated, tender ulcers with necrotic slough and undermined margins over glans penis since 5 days. The diagnosis:

[AIPGMEE '2008]

- A. Chancroid B. Syphilis
C. LGV D. Granuloma inguinale

(Ans: Chancroid)

- ▢ A 30 year-old male patient has a large, spreading and exuberant ulcer with bright red granulation tissue over

glans penis. There was no lymphadenopathy. Most likely organism in this case, is --- [AIIMS Nov' 2003]

- A. Trepanoma
- B. HSV1
- C. HSV2
- D. Calymatobacterium granulomatis

(Ans: D. Calymatobacterium granulomatis)

(This is a case of granuloma inguinale or donovonosis which is caused by Calymatobacterium granulomatis)

- C. HSV2
 - D. Calymatobacterium granulomatis
- (Ans: A. Trepanoma)

NOTES

- A 23 year - old male with h/o unprotected heterosexual contact with a commercial sex worker 2 weeks back, presents to STD clinic with painless, indurated ulcer over glans penis which exudes clear serum on applying pressure. O/E inguinal lymph nodes are enlarged and non tender. The most useful test to establish a diagnosis is
- A. Gram's staining of ulcer discharge
 - B. Darkfields microscopy of ulcer discharge
 - C. Giemsa staining of LN aspirate
 - D. ELISA for HIV
- (Ans: B. Darkfield microscopy of ulcer disc)
- This looks like a case of syphilis. Darkfield microscopy is best for diagnosis.

- 30 year male came with ulcer on glans penis associated with granuloma. On wright giemsa stain shows 1-2mm sized vacuolated round bodies in macrophage what is the cause? [AIIMS May' 10]
- A. N. Gonorrhoea
 - B. C. Trachomatis
 - C. Calymatobacterium Granulomatis
 - D. H. Ducreyi
- (Ans: Calymatobacterium Granulomatis)

- Ulcers are multiple, tender, non-indurated, bleed on touch in **chancroid** (soft sore)
- Ulcer is usually single, painless, and is indurated in **syphilis** (hard chancre or hard sore)
- Ulcer is usually single, a bright papule which bleeds on touch, a/w pseudobubo but no lymphadenopathy-- **GI**
- If pt does not present with ulcer but with painful multilocular lymphadenopathy (inguinal bubos)--it is **LGV**

A 30 year-old male developed maculopapular rash, hepatosplenomegaly 3 weeks after a h/o painless ulcer over glans penis. Most likely organism in this case, is --- [AIPGMEE 2011]

- A. Trepanoma
- B. Chlamydia

ELECTROLYTES

Sodium

	Hyponatremia	Hypernatremia
Plasma Na ⁺	< 135 mmol/L	> 145 mmol/L
M/c mechanism	↑ TBW i.e. dilutional hyponatremia	Renal water loss
Causes	G.I. losses, Diuretics , Hypoaldosteronism SIADH , TURP CRF, Nephrotic synd, Cirrhosis	Diarrhoea, dehydration Drugs , Osmotic Diuresis Diabetes insipidus (central) Decreased or absent fluid intake [<i>remember 5 'D'</i>]
C/F	Brain cell swelling or cerebral edema leads to → ↓ CBF Nausea, headache Lethargy, confusion, obtundation Stupor, seizures & coma if Na ⁺ < 120 Pulmonary edema	Hypertonic contrac ⁿ of ICF (intracellular dehydration) leads to Altered mentation Irritability/ seizures, Coma / Focal ND, M/s twitching, weakness Thirst , polyuria
T/t	Hypervolemic → Fluid & salt restric ⁿ , loop diuretics <i>If symptomatic, severe</i> → Slow correction by hypertonic saline, raise S. Na ⁺ by 12mmol/L in first 24 hr.	Allow water orally Correct water deficit $\frac{S. Na^+ - 140}{140} \times TBW$ Isotonic saline for initial correction of ECF deficit → once deficit get corrected give hypotonic saline, For central DI give clopro-pamide

- Rapid correction of hyponatremia may result in **central pontine myelinosis** or **osmotic demyelination syndrome**.
- Severe hyponatremia is serum sodium < 110 mEq/L
- **Pseudohyponatremia** is seen in **hyperlipidemia**, **hyperproteinemia**, **hyperglycemia**, **mannitol** use.
- Confusion and coma may be seen in ↓ Na⁺, ↑ Ca⁺⁺, **hyposmolarity**, **hypercapnia**.

Potassium

	Hypokalemia	Hyperkalemia
Serum K ⁺	< 3.5 mmol/L	> 5.5 mmol / L
Cause	Intracellular shift - Metabolic alkalosis, - Insulin, β ₂ agonists, α-blocker, Amphotericin B ↑ loss - Hyperaldosteronism - Cushing syndrome, - Bartter's synd - CAH,DKA - Diuretics	○ Renal failure (Both ARF & CRF) ○ A/w impaired reabsorp ⁿ of Na ⁺ hypoaldosteronism pentamidine, trimethoprim ACEi, heparin ○ Injury, sepsis, hemolysis
C/F	Fatigue, myalgia & episodic m/s weakness Hypotonia, Paralytic ileus, Abdominal distension Hypoventilation More negative RMP, ↓ DTR Metabolic alkalosis	○ Partial depolarizaⁿ of membranes results in - weakness, flaccid paralysis - hypoventilation , arrythmias Metabolic acidosis (↑ K ⁺ inhibits renal NH ₃ genesis & reabsorption of NH ₄ ⁺ , net acid excretion ↓ es).
ECG	Flattening or inversion of T-wave, Prominent U wave, ST depression & prolonged QU interval	Tall & peaked/ tenticular T-waves is the earliest change in severe hyperkalemia prolonged PRi & QRS sine wave pattern, ventricular fibrillation & asystole
T/t	Oral potchlor (KCl) is preferred If i/v K ⁺ has to be given rate should be < 20 mmol/h (not > 240 mmol/d) & ECG monitoring is must.	Ca-gluconate, Insulin with dextrose, IV NaHCO ₃ for severe cases Peritoneal dialysis, Keyoxalate resins

→ Pseudohyperkalemia occurs in patients with persistent thrombocytosis, esp in MPDs (myeloproliferative disorders), hemolysed samples.

→ Hypocupremia (Low serum copper) is seen in nephrosis, PEM, Wilson's disease, EBF infants. It is a/w neutropenia.

Calcium

	Hypocalcemia	Hypercalcemia
Serum Ca ⁺⁺	< 9mg%	> 11 mg%
A/w	Hypomagnesemia	
Causes	<ul style="list-style-type: none"> CRF Hypoparathyroidism Hypoalbuminemia VDD Rickets Acute pancreatitis <u>Tumour lysis syndrome</u> Heparin, glucagon, protamine 	<ul style="list-style-type: none"> Hyperparathyroidism, hyperthyroidism Li Cancers - breast, bronchus, kidney, Multiple myeloma, Paget's d/s of bone Sarcoidosis <u>Milk alkali syndrome</u> Thiazides, Vitamin A Prolonged immobilization
C/F	<ul style="list-style-type: none"> Depends upon cause In general ↑ neuromuscular excitability M/s spasms, laryngeal spasms Convulsions, irritability Perioral numbness, parasthesia Prolonged QTc Chvostek's, Trousseau's sign Carpopedal spasms, hyperactive DTR 	<ul style="list-style-type: none"> Short QT interval <i>G.I. symptoms</i> constipation, anorexia, vomiting, PVD, pancreatitis Polyuria, ↑ urina^a nocturia nephrocalcinosis, Depression
T/I	<ul style="list-style-type: none"> Vit D or calcitriol + high oral calcium intake I/v Ca-gluconate for symptomatic pt Thiazides 	<ul style="list-style-type: none"> Hydration Forced diuresis (frusemide) Biphosphonates Calcitonin Glucocorticoids Dialysis

Neuromuscular irritability

$$= \frac{(\text{Na}^+) (\text{K}^+)}{(\text{Ca}^{++}) + (\text{Mg}^{++}) + (\text{H}^+)}$$

i.e. in hypernatremia, hyperkalemia, hypocalcemia & hypomagnesemia neuromuscular excitability is seen & seizures may occur.

Tetany is seen in

- Hypocalcemia
- Hypomagnesemia
- Respiratory alkalosis
- Prolonged hyperventilation

→ Severe hypomagnesemia (< 0.4 mmol/L) is a/w hypocalcemia

→ About 40% of calcium is bound to albumin. So in hypoproteinemia there is ↓ in total & protein bound calcium but ionic Ca⁺⁺ is unchanged. (In hypoalbuminemia, for each gm ↓ in serum albumin below 4 mg/dl, add 1mg/dl to serum calcium)

→ M/c GI sites responsible for significant losses of -

Cl⁻ (stomach), HCO₃⁻ pancreas, Na⁺ (bile) & K⁺ (colon)

IMP. METABOLIC CHANGES

Change	Electrolytes	Seen in
Met. Alkalosis	↓ K ⁺ (Hypokalemic)	Conn's syndrome
	↓ K ⁺ ↓ Cl ⁻ (Hypokalemic hypochloremic)	Pyloric stenosis (IHPS), Gastric outlet obstruction, Prolonged vomiting, Duodenal atresia, Thiazide diuretics
Met. Acidosis	↑ K ⁺ (Hyperkalemic)	Post burn pt
	↑ Cl ⁻ ↓ K ⁺ (Hyperchloremic, Hypokalemic)	Diarrhoea, Ureterosigmoidostomy, RTA type I & II
	↑ K ⁺ ↑ Cl ⁻ (Hyperkalemic Hyperchloremic)	TPN
	↓ K ⁺ (Hypokalemic)	Large villous adenoma

- In salicylates (Aspirin) overdose there is metabolic acidosis with respiratory alkalosis.
- In cholera there is normal anion gap acidosis.
- Anion gap reflects unmeasured anions in plasma.
- Most important unmeasured anions responsible for anion gap are anionic proteins.
- Urinary anion gap is an indication of NH_4^+ ion excretion
- The most useful test for distinguishing proximal and distal RTA is measurement of urinary pH.

- Fluids useful for correction of acidosis - RL, Isolyte E, P, M
- Fluid useful to improve microcirculation - dextran 40
- Plasma expanders - albumin, hetastarch, dextran and other colloids.
- In neurosurgical cases or in a patient of stroke - NS is given and dextrose containing fluids are avoided.

FLUID THERAPY

o Dextrose - 5%:

Provides fluid & calories without electrolytes. Used in preterm neonates

o Isotonic saline (0.9% NaCl):

The best agent to treat **shock** and salt depletion.

o RL:

Most physiological fluid. Solution of choice in patients of burns, Dengue shock etc. Cautiously used in renal failure, avoided in liver failure. K^+ present in RL is 4 meq/L.

o Isolyte-M:

Best agent to provide **potassium**. Maintenance fluid.

o Isolyte-G: Only fluid to correct metabolic alkalosis and for replacement of gastric losses.

o Isolyte P: Contains electrolytes 1/2 of isolyte - M. Useful in pediatric patients.

- o 10% Dextrose means 10 gram dextrose in 100 mL. Similarly 5% dextrose means 5 gram dextrose in 100 mL. So 1 vac (500 mL) of D5% will provide 25 grams of dextrose.

- o Maintenance fluid in pediatric patients are based on Na^+ requirement, which is roughly $3\text{mEq/kg} + \text{Deficit}$. So, in a 10 kg child normal Na^+ requirement is $\sim 30\text{ meq/d}$. This requirement c/b fulfilled by N/3 or N/4 (i.e. 154/3 or 154/4)

- o **Sodium deficit** is calculated using the formula.

$$\text{Na}^+ \text{ deficit} = (135 - \text{plasma Na}^+) \times 0.6 \times \text{body wt.}$$

Hyponatremia should be corrected slowly over 24-48 hours. 1/3rd of the deficit should be corrected or replaced in first 8 hours, 1/3rd is given in next 16 hours and remaining 1/3rd over subsequent 24 hours.

- o For hypoglycemia in newborn bolus of 10% Dextrose is given in a dose of 2mL/kg.

Composition of IV Fluids per litre

Type Fluid	Electrolytes	Used in/ remark
NS or 0.9% saline (Isotonic saline)	Na^+ 154, Cl^- 154,	Shock, Dehydration, DKA
0.45% NS (Half normal saline)	Na^+ 77, Cl^- 77,	Hypertatremia
N/3, N/4, N/5		Hypertatremia
DNS	Na^+ 154, Cl^- 154, Dextrose 50gm	
0.45 DNS	Na^+ 77, Cl^- 77, Dextrose 50gm	C/b used as Maintenance fluid in children after initial correction
RL	Na^+ 131, Cl^- 111, K^+ 4, Ca^{++} 4, HCO_3^- 29,	Most physiological fluid. Preferred in Burns, dengue shock, intra-op
Isolyte P	Glu 50 gm Na^+ 25, Cl^- 22, K^+ 20, Acetate 23, PO_4^{3-} 15,	Maintenance fluid in 1-4 yr
Isolyte M	Glu 50 gm Na^+ 40, Cl^- 38, K^+ 35, Acetate 20, PO_4^{3-} 15,	Maintenance fluid in >4 yr children and in adults
10% Dextrose	Glu 100 gm	Fluid for neonates
5% Dextrose	Glu 50 gm	Initial 48 hr fluid for ELBW preterms, fluid for starvation deficit

Contraction of fluid volume

	Hypertonic Contract ^a	Isotonic contraction	Hypotonic Contract ^a
Urinary loss of	Fluid, water	Osmols or solutes + water	Mainly solutes
Plasma is	Hypertonic (Osmolality >295)	Isotonic	Hypotonic
Urine is	Hypotonic (osmolality <290)	Salt loosing	
Cause	DI	Sev.diarrhea, Salt loosing nephropathy.	Addison's d/s

→ Hypotonic expansion is seen in SIADH because of fluid retention.

→ A diluted urine with an osmolality of <300 m Osm/L supports the diagnosis of DI.

→ Third space fluid is relatively non-functional ECF volume found in burns, tissue injuries.

Causes of Metabolic acidosis

	Causes	Mechanism
Normal anion gap (10-12 mmol/L)	Diarrhea, cholera	HCO ₃ ⁻ loss
	Small-bowel fistula, Utero sigmoidostomy,	
	Proximal RTA	↓ Tubular reabsorp ⁿ of HCO ₃ ⁻
	Distal RTA	↓ acid excretion
	Acid (NH ₄ Cl, HCl) administration	↑ acid load
High (wide) anion gap acidosis	"Dilutional" acidosis	Volume expansion with HCO ₃ ⁻ free fluids
	Intestinal obstruction	
	Shock, Lactic acidosis (phenformin)	↑ lactic acid
	Diabetes (DKA), starvation, alcohol	↑ keto acids (Ketoacidosis)
	Uremia (ARF & CRF)	Retention of sulfuric, phosphoric acids
	Ingestion of methanol, salicylates, ethylene glycol (anti-freeze), aspirin	Conversion to formic, oxalic and salicylic acids respectively

→ Anion gap is low in ---multiple myeloma, bromides, iodides, etc.

WOUND

Types of Wound

- **Clean**
 1. An elective procedure with no infection
 2. Surgery in which resp/alimen/ urinary/ genital tract is not entered
 3. No breach in aseptic precautions.

Risk of contamination is about 24 hours after the operation for most wounds. Wounds are covered with sterile dressings to reduce the risk of such contamination.

- **Clean contaminated**
 1. Minor breach in aseptic precautions
 2. Resp/alimen/ urinary/ genital tract is entered with minimum spillage

- **Contaminated**
 1. Major breach in aseptic precautions
 2. Gross spillage with resp/alimen/ urinary/ genital tract

- **Dirty or infected**
 1. All traumatic wound of >4hour duration
 2. Preop-contamination with visceral contents.

Clean wounds have a 1%-5% risk of infection; clean-contaminated, 3%-11%; contaminated, 10%-17%; and dirty, over 27%

WOUND HEALING

- **Phases of wound healing ---**
 1. Inflammation --- 4-6 days
 2. Proliferative --- 7-42 days (80-90% strength is achieved in 30 days)
 3. Remodelling --- 42 days-2 yrs
- In tidy wounds (e.g. wounds of surgical incision and clean incised wound caused by sharp objects) usually **primary suturing** is done within 6 hrs. Healing occurs by primary intention.
- **Delayed primary suturing** is done in 4-5 days of wounding in case of lacerated wounds. This time is allowed for infection and edema to subside.
- **Healing by secondary intention** occurs when primary suturing done in the past.
- **Tensile strength of wound ---**
 1. At 1 week 10% of normal
 2. At 3 months it is 90% (maximum)

Needles for Biopsies

- 14 G → Core Bx
- 18 G → Liver Bx in Cirrhosis
- 22 G → FNAC
- *Fogarty catheter* is used for removal of fresh clot embolus in artery.

INJURIES

- Rule of Conservative treatment
 1. 85% of thoracic trauma requires --- conservative t/t
 2. >90 % of renal trauma require --- conservative t/t
 3. >85% of hepatic trauma requires --- conservative t/t
- 10% of patients require thoracotomy in thoracic injuries
- Missile injury always require laprotomy

Indications of Thoracotomy

- Blood >1500 mL in chest tube
- Blood > 200 mL/hr for >3 hour in chest tube
- Foreign body > 1.5 cm in diameter
- Cardiac tamponade
- Intubation is done when GCS is < 8/15
- In case of blast injuries cavitation in solid organs indicates --- increased mortality.

MISSILE INJURIES

- A high velocity missile from a modern high velocity rifle, causes an explosion in the tissues with extensive cavitation. Small entry and exit wounds may conceal gross damage inside.
- The wounds from standard rifle bullets are least likely to be infected, because firing will have sterilized them and they do not cause much tissue destruction.
- The lung is remarkably resistant to missile injuries. Drain a haemothorax or haemopneumothorax.
- T/t: TT prophylaxis, fasciotomy, control all bleeding, leave the wound open (except for face wounds which can be closed immediately), and cover it with gauze.

HAND SURGERY, FOOT

No man's land

Zone from the middle of the palm to just beyond the PIP joint, where in the superficialis and profundus lie ensheathed together

and where recovery of glide is so difficult after wounding.

Parona's space

Is the tissue plane over the **pronator quadratus** in the distal forearm deep to radial and ulnar bursa.

Felon

- Infection of volar distal fat pad (terminal pulp space) of the finger usually after splinter / needle prick injury
- Local pain and lymphangitis present ; osteitis may occur
- R_x : I & D ; longitudinally oriented incision is given to divide fibrous septa

Ainhum/ Autogangrene

- A fissure appears at level of interphalangeal joint of toe usually the **5th toe**
- Unknown etiology, affects black males
- T/t : Z-plasty

Paronychia

- Painful infection of radial / ulnar sides of nail
- If suppuration occurs --- nail should be removed

→ *Most imp. structure to be repaired in hand injury --- skin.*

→ *Structure first to be repaired in hand injury --- vessel*

→ *Median nerve by its sensory innervation is "the eye of the hand".*

ULCERS & SWELLINGS

- **Shea** classification is used for pressure sores /pressure ulcers.

Trophic ulcers

- D/to impaired nutrition, defective blood supply, neurological deficit (so also k/as **neurogenic/ neuropathic ulcer**)
- *Neurological causes are* – Diabetes, peripheral neuritis, tabes dorsalis, spina bifida, **leprosy** (Hensen's d/s), spinal injury, paraplegia, syringomyelia.
- Bedsores are trophic ulcers
- Trophic ulcers are painless, punched out ulcers

→ *5 'p' of granulation tissue – pink, punctate hemorrhage, pulseful, painless, pin head granulation*

→ *Mantorelle's ulcer are seen in calf region and are d/to hypertension and atherosclerosis*

Ulcers & Types of edges

- Everted (rolled out edge)/ -- SqCC, epithelioma, carcinoma heaped up
- Undermined edge -- Tuberculous ulcer
- Sloping edge -- Healing ulcer
- Punched out edges -- Peptic Ulcer
- Punched out edge with thin-- Syphilis (Gummatous base + wash leather slough ulcer)
- Raised & beaded edge -- BCC (Rodent ulcer) (pearly white)
- Collar button/stud ulcer -- In Crohn's d/s
- Sloping edge -- Healing ulcer
- *Some punched out ulcers:*
 - Mortorell's ulcer found in leg in poorly controlled HTN.
 - Deep trophic ulcer
 - Peptic ulcer
 - Syphilitic/ gummatous ulcer (thin base + wash leather slough)

→ Cortisol ulcers are callous ulcers with no healing tendency. These are d/to long term application of steroids.

→ Collar button (Collar stud) ulcers in mucosa & submucosa of colon are seen in Crohn's d/s.

ABSCESSSES

- Visible (pointing) pus, tenderness and fluctuation are the features of formed abscess. Require I & D.
- Abscess are drained by giving incision at the site of maximum pointing (Hilton's method)
- Abscess should be formed before draining (exceptions are -- parotid, breast, axillary, thigh and ischioirectal abscess)
- Abscess drainage :
 - Non viscous (cyst, ascites) --- 6-10 Fr.
 - Thick inspissated --- Saline irrigation with double lumen catheter.

Antibioma

Is common in breast abscess. It is formation of thick granulation tissue with fibrosis surrounding the abscess cavity. It is d/to prolonged use of antibiotics.

Cold Abscess

No sign of acute inflammation is seen (i.e. it is not red/ warm/ tender). It is d/to tuberculosis. Non dependent aspiration + ATT is TOC. Drain is not placed in cold abscess. (high risk of sinus formation)

Collar stud abscess

An acute suppurative infection of a digit /LN presenting as a stud-like blister. The abscess tracks to deeper tissue; hence, simple incision of the blister will not resolve matters. Exploration & delayed closure required. Systemic antibiotics are recommended. Also seen in **tubercular cervical lymphadenitis**.

CYSTS

- *Congenital :*
 - Dermoids, thyroglossal cysts, urachal cysts.
- *Acquired :*
 - Retention cysts* ---Sebaceous cysts, Bartholin cysts, parotid/ breast cysts
 - Distention cysts*---Ovarian cysts, lymph cysts, colloid goiter
 - Exudation cyst* --- Hydrocele
- *False cysts:*
 - Have no epithelial lining (e.g. pseudocyst of pancreas, haematoma etc.)

→ Plunging ranula is an example of retention cyst.

Swellings which are brilliantly transilluminant

- Ranula
- Cystic hygroma and lymph cyst
- Primary hydrocele
- Epididymal cyst
- Meningocele

Swellings which are cross-fluctuant

- Psoas abscess
- Bilocular hydrocele
- Ranulla (plugging)
- Compound ganglion of palm

SURGICAL INFECTIONS

Cellulitis

Non-suppurative spreading inflammation of subcutaneous and fascial planes mainly d/to *Streptococcus pyogenes*. Other organisms implicated are - *Staph.*, *H.influenzae*, *bacteroids*.

- *Impetigo (Pyoderma)*

Is a superficial infecⁿ of the skin caused mainly by group A streptococci

- *Erysipelas*

Is spreading inflammation of skin and subcutaneous tissue d/to streptococcus pyogens. Erysipelas can spread to pinna (cuticular infection) of ear and produce Milian's ear sign [Remember mnemonic: *Strepto NICE* (*Streptococcus causes Necrotising fascitis, Impetigo, Cellulitis, Erysipelas*)]

- *Boil (Furuncle), Folliculitis*

Is an acute staphylococcal infection of hair follicle with perifolliculitis

- *Hidradenitis suppurativa*

Is chronic infection of apocrine sweat glands involving group of follicle.

- *Carbuncle*

Infective gangrene of skin and subcutaneous tissue mainly d/to localized *staphylococcal infection*. Commonly seen in diabetic and immunocompromised patient.

→ *Staph. infection is localised in carbuncle while it is generalised in SSSS, TSS.*

→ *Pott's puffy tumour is diffuse external swelling in the scalp d/to subperiosteal pus/ acute osteomyelitis of frontal bone.*

Post op infections

- M/c cause of surgical site infection (SSI) --- Staph aureus.
- M/c cause of fever in post op period --- UTI
- M/c cause of late cause of fever in post op period --- thrombophlebitis.
- Rate of surgical wound infection:
 - Cholecystectomy 3%
 - Inguinal herniorrhaphy 2%
 - Appendectomy 5%
 - Thoractomy 6%
 - Colectomy - 12% (Highest)
- Fever + ileus + shock are the signs of organ space SSI.
- 1st step in the m/m of SSI- reopening the wound or, in the case of deep space infections, using techniques that are guided by CT or US for drain placement.

HIV infection in Surgical patient

- Use of double gloves decreases the risk.
- Use of hollow needle carries more risk than solid needle.
- M/c cause of laparotomy in surgical pt --- CMV infection.

ARTERIAL DISORDERS

5'P' of sudden arterial occlusion (embolic)

- Pain
- Pallor
- Paresthesia
- Paresis
- Pulselessness

BUERGER'S D/S (Thromboangiitis obliterans)

- Char/by occlusion of **small** and medium sized arteries, thrombophlebitis of superficial or deep veins, and Raynaud's phenomena. (But not a/w atherosclerosis)
- D/s starts in plantar/palmar, radial arteries with proximal progression. Plantar ---Tibial arteries are **m/c** site
- Affects males of <30 years of age.. Smoking is a risk factor
- Angiography sometimes show "corrugation" of femoral arteries
- Gangrene of the toes and fingers is common and progressive.
- Histologically : Panangiitis
- T/t: Abstinence from smoking. Lumbar sympathectomy to relieve rest pain, gangrenous frost, ulcer. Amputation for persistent pain

INTERMITTENT CLAUDICATION

- Cramp like pain d/to decreased blood flow (**ischemia**) to arteries. **Calf** region is the **m/c** site. A/w atherosclerosis and smoking.
- Pain is brought on by walking but does not occur on taking first step (unlike osteoarthritis), relieved by standing still (unlike lumbar disc compression)
- Lumbar sympathectomy is contraindicated.

SYMPATHECTOMY

- In **Lumbar** sympathectomy L₂ L₃ L₄ are removed (L₁ ganglion on one side should be preserved, if bilateral L₁ is removed impotence may result d/to failure of ejaculation).

Indications are

- Causalgia
- Arterial occlusive d/s e.g. **Buerger's d/s** for
 1. Rest pain
 2. ischemic ulcers
 3. gangrenous frost
- Symptomatic vasospastic d/s
- Plantar hyperhidrosis
- o Contraindication to L~ is --- Intermittent claudication
- o **Thoracic sympathectomy** ---for palmar hyperhidrosis
- o **Cervical sympathectomy**--- for Raynaud's d/s, acrocyanosis

Causalgia

- o Occurs after partial nerve transection
- o There is severe burning pain, skin hypersensitivity may make contact with clothing intolerable.
Coolness, cyanosis, hyperhidrosis & edema are also characteristic of the syndrome.
- o Cervical sympathectomy provides *pain relief*

→ *Popliteal artery aneurysm is m/c peripheral arterial aneurysm*

Ankle-brachial pressure Index (ABPI)

- o Ratio of SBP at the ankle to that in the arm.
- o Normal value ~ 1.0
- o ABPI <0.9 is considered diagnostic of PVD and is a/w >50% stenosis in at least 1 major LL vessel. If <0.3 → indicates imminent necrosis

AORTIC DISSECTION

- o M/c cause - HTN.
- o M/c site - Distal aorta.
- o Risk increases with - EDS (Ehler Danlos syndrome), Marfan's, cystic medial necrosis.
- o M/c symptom - pain.
- o Stanford or De Bakey classification is used.
- o Blunt chest trauma usually causes dissection of the ascending aorta and/or the region of the ligamentum Botalli at the aortic isthmus.
- o ECG is the 1st step to rule out ischemia.
- o Beta blockers (Esmolol, propranolol) useful in t/t.
- o Cardiac tamponade is the m/c cause of death from aortic dissection.

THORACIC OUTLET SYNDROME

- o Selmonosky's triad: Supraclavicular tenderness + Hand paleness on elevation + weakness of 4th/5th finger.
- o Pressure (compression) symptoms on these blood vessels or nerves (brachial plexus).
- o Pressure may happen if there is an extra rib, above the first one or an abnormal tight band connecting the spine to the ribs.
- o Arterial thoracic outlet syndrome is caused by the compression of the subclavian artery by a cervical rib (*Cervical rib syndrome/ Subclavian steal syndrome*): BP in the affected arm is low. Doppler ultrasound is IOC.
- o Venous thoracic outlet syndrome: Results from the compression of the subclavian vein. Accounts for about 4% of all cases. Claudication, edema, cyanosis, and venous dilatation may be present.

VENOUS DISORDERS

Clinical Tests for varicose veins

Test for	Name of the test
Saphenofemoral incompetence	Trendelenberg I, Morrissey's cough impulse test
Perforator incompetence	Trendelenberg II, Multiple tournique test, Schwartz test (valve patency check)
Patency of deep veins	Modified Perthes test

- *If Perthes test is +ve, it is a contraindication for surgery*
- *Perforating veins have valves near their origin and at their entrance to deep veins. Under normal conditions they allow blood to flow only from superficial → deep veins (unidirectional).*
- *Varicose veins develop when the blood leaks continuously from high pressure deep venous system and is allowed to enter the → low pressure & poorly supported superficial venous system.*
- *SEPS (Superficial endoscopic perforator surgery) is done for --- venous ulcers*

C/c of varicose veins

- o Venous ulceration: over medial malleolus; brownish pigmentation is early sign.
- o Superficial thrombophlebitis, lipodermatosclerosis, ankle edema.
- o CEAP Classification is used for venous diseases of leg/varicose veins.

VENOUS THROMBOSIS

Risk factors for venous thromboembolism

Acquired	Genetic
- Obesity	- Genetic factor V Leiden mutation
- Cigarette smoking	- Prothrombin gene mutation
- HRT	- Def. of AT-III, protein C&S.
- OCPs/Pregnancy	- PAI-1 excess
- Trauma - Surgery	
- TTP, PNH, PV	
- Hyperlipidemia, paraproteinemia, DM	
- Cancer	
- Systemic arterial HTN	
- Antiphospholipid antibody synd (Lupus anticoagulant)	
- Bechet's syndrome, Homocystinuria	

DVT or Phlebothrombosis

- M/c site is calf vein. (Soleal m/s venous sinuses are m/c sites for initiation of venous thrombosis)
- Triad of venous stasis + endothelial injury + hypercoagulable states (*Virchow's triad*) poses a risk factor.
- **Homan's sign** positive (dorsiflexion of foot produces pain in calf); Moses test
- Venography is the most accurate & gold standard method of confirming DVT & its location.
Modern investigation of choice for the d/g of DVT is duplex ultrasound imaging (colour doppler)

Risk factors for DVT

- Prolonged bed rest/ immobility, pregnancy, puerperium, OCPs/estrogens,
- Debilitating illness, **obesity**,
- Trauma,
- Thoracic/ abdominal surgery, post-op states
- **Hypercoagulable states** (Factor V Leiden mutation, Deficiency of antithrombin III, Protein C / S deficiency, Homocystinemia, Antiphospholipid syndrome)
- The m/c inherited thrombotic disorders include Factor V Leiden (activated protein C resistance).

Prophylaxis for DVT

- Reduce obesity, mobilise early, adequate hydration, walking.

- Low dose heparin / unfractionated heparin (5000 U s/c), warfarin and external pneumatic compression. Warfarin in a dose that yields INR of 2.0 to 3.0
- Danaparoid (a LMW heparinoid) in patient undergoing hip surgery.
- Fondaparinux capable of catalyzing AT mediated inhibition of X_a is useful in orthopedic surgeries
- Aspirin
- T/t
Standard t/t is i.v. heparin for at least 5 days, dose is adjusted acc/to weight and APTT.
Warfarin is indicated to prevent further recurrence and its dose are adjusted acc/to PT and INR.

Warfarin anticoagulation

- Warfarin/ oral anticoagulation should be stopped 7 days prior to any surgery (like tooth extraction) and PT should return to normal level.
- Effects of warfarin are reversed by inj. Vit. K_1 , the dose of vitamin K_1 depends on INR and emergency of reversal.

M/m of warfarin overdose

- The INR is a test of blood clotting, which is primarily used to monitor warfarin therapy, where the aim is to maintain an elevated INR in a certain range eg, 2.0 to 3.0.
- If INR <5 but > therapeutic range → Discontinue warfarin temporarily.
- If INR 5-9 → Vitamin K1
- If INR >9 but no bleed → Vitamin K1 (3-5 mg)
- If INR >20 or active bleed → FFP

→ Dose of heparin is adjusted/ monitored by APTT

→ Warfarin effects are measured by INR.

→ The dose of oral anticoagulants (*Warfarin/ coumarin/ phenindione*) is adjusted by PT (prothrombin time) and INR.. INR is a better test to monitor the effect of oral anticoagulants.

→ A standardized system to monitor patient has been developed using human brain thromboplastin and it is k/as INR. desired value for DVT prophylaxis 2-2.5, T/t of DVT, PE/ TA, hip surgery 2-3, Recurrent thromboembolism, MS, prosthetic heart valves 3-4.5

→ Assessment of LMWH activity require assesment of Anti- X_a levels.

HEAD & NECK

Branchial Cleft Anomalies

	Branchial cyst	Branchial fistula (sinus)
Develops from	Remnant of 2nd branchial arch/ cleft	Represents a persistent whole 2nd branchial cleft
Lined by	Squamous epithelium	Squamous epithelium
At the anterior border of sternomastoid, Located at the junction of	Upper 1/3rd + lower 2/3rd	Upper 2/3rd + lower 1/3rd (external orifice)
C/F	Fluctuant, transillumination usually -ve, Toothpaste like material present, contains cholesterol crystals	Sinuses are more common than cyst
4. T/t	Sx	Complete surgical removal is always indicated.

Thyroglossal Cyst Vs Thyroglossal Fistula

Thyroglossal Cyst	Thyroglossal fistula
<ul style="list-style-type: none"> ◦ Congenital ◦ Present anywhere along thyroglossal tract ◦ M/c site is subhyoid ◦ Moves upward on protrusion of tongue as well as on swallowing 	<ul style="list-style-type: none"> ◦ Always acquired following infection/ inadequate cyst removal. ◦ Median fistula of neck. ◦ Moves upward on protrusion of tongue ◦ R_x Sistrunk operation.

→ A papillary thyroid carcinoma can arise in a thyroglossal cyst.

→ Initial investigation in discrete thyroid swelling - FNAC.

C/c of total thyroidectomy

1. Hemorrhage : A tension hematoma deep to cervical fascia develops d/ to slipping of ligature on the superior thyroid artery. T/t is immediate removal of sutures of deep fascia
2. Respiratory obstruction : D/ to collapse or kinking of the trachea. Most cases are d/to laryngeal oedema, tension hematoma (t/t is needle tracheostomy using 12G)
3. RLN paralysis : in 3% subjects it occurs and leads to hoarseness of voice.
4. Thyroid insufficiency (20-45%) : Occurs usually after 2 years.
5. Parathyroid Insufficiency (0.5%) : Present after 2-5 days

of operation usually but delayed upto 2-3 wk with marked hypocalcemia which is asymptomatic. Cause is infarction of parathyroid gland d/to loss of blood supply via inferior thyroid artery

6. Thyrotoxic crisis (Storm)

Seen in patients with uncontrolled hyperthyroidism who undergone thyroidectomy. C/by hyperpyrexia, dehydration, restlessness. T/t is I.V. fluids, cooling with ice packs, O₂, diuretics for cardiac failure, Digoxin for atrial fibrillation, Sedation and hydrocortisone, carbimazole, Lugol's iodine, sodium iodide, propranolol etc.

→ During postoperative period serum calcium levels are measured within 24 hours of surgery to detect parathyroid insufficiency.

→ In 25% patient transient hypocalcemia develops and if associated with severe symptoms than i.v. calcium gluconate is to be given otherwise oral calcium c/b given

Types of Neck Dissection

	RND	MRND
◦ Structures removed	Type I to V neck nodes, Accessory spinal n., IJV, Submandibular glands, Sternocleidomastoid m/s	Types I to V
◦ Structures preserved/saved	Nil	Type I - Accessory spinal n. saved II - Ac n. + IJV III - Ac n. + IJV + SCM
◦ Complication	Injury to Ac. nerve → trapezius paralysis → Drooping of shoulder	Less

[RND = Radical Neck Dissection; MRND = Modified RND]

Mnemonics of structures saved

- RND - Nil
- MRND type I - A
- MRND type II - AI
- MRND type III - AIS
- Elective or selective ND is removal of > 1 major LN group along with preservation of SIA. It is usually done for primary cancer that has > 30% chances of occult metastasis Used for N₀ d/s.

BREAST

Types of Mastectomy

	Patey's or MRM	RM	ERM
Structures removed	Breast & associated structures (including nipple, areola) dissected 'en bloc'	Same as MRM + Pectoralis major	RM + Ribs, LN
Structures preserved	Axillary vein Bell's long thoracic nv Cephalic vein Nerve to latissimus Dorsi & pectoralis major	ABC	

- SRM (Super radical mastectomy) is ERM (Extended radical mastectomy) + removal of supra-clavicular and mediastinal LN.
- Sentinel node biopsy is done in patients with clinically node negative d/s.

ESOPHAGUS

Boerhaave syndrome

- Caused by forceful vomiting and retching against a closed glottis.
- Cricopharynx & pylorus are closed. Intra-gastric pressure is very high → pressure builds up in the esophagus → Barotrauma results
- Site of tear: Transverse perforation in posterolateral part of lower end of esophagus (left lower esophagus)
- Full thickness (complete) tear** (through and through tear in lower esophagus) no hematemesis.

Mallory - Weiss tear / syndrome

- Partial thickness tear** below GE junction (below cardia) in 90% cases. Only in 10% cases tear is in esophagus..
- Another barotrauma. Pylorus closed, LES closed
- Vertical tear in cardia
- Tear is partial thickness involves mucosa + sub-mucosa.
- Seen in alcoholic/bulimia nervosa patients.
- Vigorous vomiting produces a **vertical (longitudinal) tear**. Usually presents with hematemesis requiring endoscopic therapy.
- Inv: UGIE (upper GI endoscopy)
- 2/3rd patient are a/w hiatus hernia (which is located on great curvature side).
- T/t is usually conservative. Sx is required rarely.

- M/c common site of iatrogenic esophageal perforation --- Cervical esophagus or cricopharynx.
- Plummer Vinson syndrome is iron deficiency anemia + glossitis + esophageal webs.
- M/c site of esophageal webs --- upper esophagus.
- M/c common site of esophageal rings --- lower esophagus.
- M/c site of esophageal carcinoma --- lower 1/3rd
- Best way to visualise esophageal swallowing --- Videofluoroscopy.

Barret's Esophagus

- Premalignant condition for Ca esophagus.
- Presence of columnar epithelium 3 cm above the GE junction.

Pneumomediastinum

- Hamman's crunch / sign are present in pneumopericardium. d/to cracking sound on auscultation with each heart beat.
- Inv: Contrast radiography.
- T/t: Surgery.
- Mackler's Triad: Vomiting + chest pain + s/c emphysema seen in esophageal rupture.

Dysphagia lusoria

- Constriction of esophagus by aberrant vessel (**Rt subclavian artery**, which arises distal to right subclavian a.) vascular ring or double aortic arch.
- Inv: Contrast radiography
- T/t: Complete excision and reanastomosis.

Esophageal Webs

- Seen at the l/o cricopharynx.
- Asymmetrical mucosal webs**, seen in post menopausal females.
- A/w IDA, Plummer Vinson syndrome.
- Can cause dysphagia occasionally (**sideropenic dysphagia**).

Schatzki rings

- Symmetrical sub-mucosal thickening** at the lower thoracic esophagus above the diaphragmatic indentation.
- A/w hiatus hernia.
- Seen at the squamocolumnar junction.
- C/F: Non-progressive dysphagia or sudden aphagia.
- T/t: Ballon dilatation.

STOMACH

- *Hourglass stomach* is chronic complication of *lesser curve ulcer* usually seen in women, a/w *pyloric stenosis*, clinically silent. T/t is Billroth I gastrectomy
- *Watermelon stomach* is seen in old females. Mucosa develops too much vascular erosion. Involves **antrum**. T/t is antrectomy. Usually a/w CLD (chr. liver d/s). C/F hematemesis.
- *Meteorism* is acute sudden gastric dilatation seen in hypokalemia, septicemia, uremia [conditions which predisposes to paralytic ileus].
- *Ménétriér's disease*
 - Autoimmune hypertrophic gastritis c/by hypertrophied or giant gastric rugae; excessive loss of protein from the gut which results in hypoproteinemia.
 - Mucosal cells ↑, all other cells ↓
 - Etiology : Altered expression of TGFα.
 - C/f : edema, diarrhoea, anorexia, chronic bld loss.
 - Premalignant condition seen in females. There is ↑ risk of adenocarcinoma. So treated by total gastrectomy.

H.pylori infestation

- Gram -ve, urease producing bacteria a/w
 - Duodenal ulcer
 - Gastric ulcer
 - Maltoma
 - Carcinoma.
- H.Pylori colonises only in stomach mucosa not duodenum or esophagus.
- Stained by Silver Warthin stain.
- Causes
 - Cancer in body
 - Ulcer in antrum
 - Gastritis in antrum (Type B)

M/c site in stomach

- Lesser curvature : M/c site for gastric ulcer (esp post. wall of LC)
- Fundus : *Ménétriér's* ds, Ca following pernicious anemia.
- Body : Silent Ca, M/c site of Carcinoma
- Pylorus-antrum : M/c site of Linitis plastica

→ *Prepyloric region* along greater curvature is the m/c site for gastric carcinoma.

Peptic Ulcers

- *Curling ulcers* are stress ulcers commonly seen in severe burns or trauma. Location - proximal duodenum.
- *Cushing ulcers* are gastric, duodenal and esophageal ulcers seen in patients of head injury, cranial surgery, or tumours. It carry high incidence of perforation.
- M/c site of ischemic ulcers → fundus.
- Duodenal ulcers bleed posteriorly.
- Peptic perforation occurs in the anterior aspect of duodenum.

Duodenal Ulcer versus Gastric ulcers

DU	GU
• Most DU are found in first part of duodenum usually just post- pyloric & more commonly on anterior wall than posterior	• GU are found predominantly <u>along the lesser curvature</u> in pyloric antral region more commonly on posterior than anterior wall
• In DU perforation usually occurs from <i>ant. wall</i>	• GU perforation are rare than DU But if they occur they are seen posteriorly into lesser sac.
• <u>Bleeding is the m/c complication</u> & also m/c cause of death. Occurs from post wall d/to involvement of gastroduodenal artery	• Bleeding is due to erosion of Lt gastric a. > splenic artery.
• Pain relieved by food	• Pain aggravated by food & relieved by antacids
• Weight gain	• Weight loss
• <u>Never</u> turns malignant	• Ulcers along lesser curvature are benign & along greater curvature are more malignant
• Blood gp O association ['o' in duo]	• Blood gp A association ['a' in Gastric & also in gastric carcinoma]
• Increased BAO & MAO	• Normal to ↓ BAO & MAO

Operations for Peptic Ulcers

Operation	Recurrence rate %	Complication rate
• Vagotomy + antrectomy (Billroth I or II)	1	Highest (II>I)
• Vagotomy and pyloroplasty	10	Intermediate
• Proximal gastric vagotomy/parietal cell V~/Highly selective V~	≥ 10	Lowest (best)

[Billroth I = gastroduodenostomy; Billroth II = gastrojejunostomy.]

- *M/c recommended surgery for DU with intractable pain* ---Parietal cell vagotomy
- *M/c surgery for DU with obstruction* ---Vagotomy + gastrojejunostomy
- *M/c surgery for DU with perforation*--- Omental patch [Graham's patch]
- *C/c of vagotomy*→ Delayed gastric emptying

INTESTINE

- *M/c site of congenital duodenal diverticulae* --- IInd part of duodenum.

Duodenal obstruction

- Seen in
 - Duodenal atresia (*M/c* symptom is bilious vomiting). TOC is D-D stomy (duodeno-duodenostomy).
 - Annular pancreas (TOC is D-J stomy)
 - Ladd's band.
- Double bubble sign is seen.

Parts of intestine m/c affected in d/s or infestations

D/s or infestation	Part
1. TB 2. Typhoid ulcers 3. <i>M/c</i> site of carcinoid tumour in GIT	Ileum
Shigellosis	Colon
Volvulus Amoebic Colitis, Diverticulosis	Sigmoid colon
1. <i>Campylobacter jejuni</i> infesta ⁿ 2. Commonest site for FAP, colorectal ca.	Recto-sigmoid
1. Carcinoid syndrome 2. Polyps of Peutz-Jegher's syndrome	Jeuno-ileal

Site for crohn's ds, Gallstone ileus, obstruction in meconium ileus.	Terminal - ileum
Intestinal TB	Ileo-cecal region
Amebiasis (ulcers & perforation)	Caecum
<i>Enterobius vermicularis</i>	Appendix
Bleeding in angiodysplasia	Right colon
Bleeding in diverticula	Ascending colon
Toxic megacolon (in IBDs)	Transverse colon
Ischemic colitis	Splenic flexure
UC, Hirschsprung's d/s.	Rectum

Intestinal obstruction

- Hirschsprung's d/s is the *m/c* cause of lower intestinal obstruction in neonates (incidence is 1 in 5000).
- Intussusception is the *m/c* cause of intestinal obstruction b/n 3 months - 6yr of age in children
- Post operative adhesions makes up 60-80% of admissions for small intestinal obstruction (commonest cause) in adults. Next are Hernias 15-20%, malignant tumours 15-20%.
- Colonic obstruction most often arises from cancer (60%) diverticulitis (15%) or volvulus esp in elderly.
- Overall *m/c* cause of intestinal obstruction is paralytic ileus (adynamic ileus).
- Post-operative paralytic ileus is *m/c* seen in → ileum.
- *Mirizzi syndrome* → Extensive obstruction of CBD from cystic CBD stones.
- *Ogilvie syndrome* → Acute colonic pseudo-obstruction (ACPO), also k/as Ogilvie's syndrome, is a condition c/ by idiopathic massive colonic distension in the absence of any mechanical obstruction in severely ill patients

Peritoneum

- Bile, gastric juice, pancreatic juice all are peritoneal irritant. Blood is least irritant.
- SBP (Spontaneous bacterial peritonitis) is common in children. Caused by streptococcus pneumoniae.
- *Lenk's triad* is seen in retroperitoneal hemorrhage. C/ by flank pain + palpable tender mass + signs of internal bleeding.
- *M/c* site of pelvic abscess : Pouch of Douglas ((R.uteri).
- *M/c* site of subphrenic abscess : Morrison's/Hepatorenal Pouch.

Intestinal Fistulae

- Small intestinal fistula is m/c after operations, Crohn's disease accounts for < 2%.
- Fistulae and sinuses are rare in UC.
- Diverticulosis can cause fistula formation, haemorrhage, intestinal obstruction, peritonitis, etc.

Meckel's Diverticulum (MD)

- M/c cause of lower GI bleeding in infants and children.
- Rx :
 - MD with ectopic tissue → Resection and anastomosis.
 - MD without ectopic tissue → Diverticulectomy and wedge resection of ulcer.
- MD is a congenital diverticulum so it has all the 3 layers of intestine.

Acute Mesenteric Ischemia

- M/c cause : Embolus (arterial in 75% cases).
- M/c artery involved : SMA.
- M/c site : Splenic flexure (Griffith's point), Sudeck's point (b/w sigmoid and rectum).

G.I. BLEEDING

Acute Upper GI Bleed

- I/v vasopressin is usually avoided.
- Endoscopic ligation is diagnostic as well as therapeutic.

Lower GI Bleed

- Amoebic dysentery is the m/c cause of lower GI bleed in India.
- Important causes: by age group in order of frequency

Infants & Children	Adolescents & young adults	Adult - 60yr.	> 60 yrs.
Meckel's diverticulum	MD	Diverticulosis	Vascular ectasias (angiodysplasias)
Polyps	IBD	IBD	Diverticulosis
UC	Polyps	Polyps	Malignancy
Duplication		Malignancy	Polyps
		Cong. A-V malformation.	

→ Colonic bleeding from angiodysplasia is best diagnosed by arteriography or colonoscopy.

→ Colonic bleeding most often results from polyps / neoplastic disease. Usual presentation is that of unexplained anemia.

INFLAMMATORY BOWEL DISEASES (IBDs)

CD & UC share some common features :-

- Both are chronic, relapsing IBDs of unknown etiology.
- Mucosal inflammation+.
- Extraintestinal manifestations are more common in UC : Arthritis (commonest), erythema nodosum, uveitis, sclerosing cholangitis, sacroiliitis, ankylosing spondylitis, pyoderma gangrenosum, iritis, bile duct cancer (cholangiocarcinoma).
- Rectal involvement, toxic megacolon, collar stud (Collar button) ulceration, crypt abscesses, pseudopolyps more in UC than CD. Rest of the features are more in CD.
- Small bowel obstruction occurs in ~27% of patients and is the m/c cause of morbidity in UC patients.

	CD	UC
Involvement	Discontinuous/ Segmental / patchy with skip lesions	Continuous
Starts in	Terminal ileum (terminal ileitis), but may involve any portion of GIT.	Rectum, extends retrograde to involve colon (Backwash ileitis)
Involvement	Transmural (fistula, anal fissures, sinuses are common)	M + SM
Ulcers	Serpiginous	Superficial ulcers only
Other/F	Fibrosis +	Rare
	Strictures +	Never
	Fistula & sinuses +	Rare
	Hose-pipe & Cobblestone appearance	Pseudopolyps [GARDEN HOSE APPEARANCE]
Radiograph	String sign in terminal ileum "Creeping fat".	1st sign → Loss of haustral markings, short bowel (b/of fibrosis)
Micro	Non-caseating granuloma (Sarcoid like)	Crypt abscess
Cl/F	Intermittent RLQ colicky pain with diarrhea / bleeding is the m/c symptom.	Frequent bloody bowel movements with mucus. LLQ cramping pain, (Tenesmus)
C/c	↑ Risk of perianal ds, Malabsorption	Dysplasia / colorectal adenocarcinoma Toxic megacolon, Perforation

- o Earliest radiological/ Ba-enema finding in UC:
Loss of mucosal lining (blurring) → Loss of haustrations
→ Lead pipe appearance → Pseudopolyps.
- UC starts in Rectum, M/c site of involvement in UC is Rectum,
M/c site of toxic megacolon is transverse colon and loss of
haustrations on barium enema are typically seen in distal
colon.
- T/t of UC : steroids are most useful (for acute
exacerbations) and best for small bowel disease.
Sulfasalazine for maintenance of remission & more effective
for colonic (than small bowel) ds.

INTESTINAL TUBERCULOSIS

- o TB can affect any part of g.i.t from the mouth to anus.
- o M/c site of abdominal tuberculosis is ileocecal region d/ to
presence of abundant Peyer's patches and stasis.
- o There are 3 forms of I~
– Ulcerative
– Hyperplastic
– Mesenteric
- o M/c organism now a days is M.tuberculosis hominis.
- o Salient features of these are compared in the table.

	Ulcerative TB	Hyperplastic TB
Cause	2° to pulmonary TB	2° TB, could be d/ to bovine TB
Body resistance	Poor	Good
Patho	Multiple transverse ulcers	Chronic granulomatous lesions
Cl/f	Diarrhea, PR bleeding, loss of appetite	Mass in Rt iliac fossa, which mimics ca-caecum
C/c	Stricture, obstruction	Obstruction, surgery required
Ba meal follow	Filling defect in lower ileum, Pulled up caecum, obtuse ileoceleal angle, dilated proximal loops	Long narrow filling defect in terminal ileum,
T/t.	ATT.	Surgery is TOC (Limited hemicolectomy i.e. removal of ileocolic junction + ileo-ascending anastomosis).

DIVERTICULOSIS

- o M/c site of diverticulosis is colon : In 90% of cases sigmoid
colon is involved. In small intestine 2nd part of duodenum
is the m/c site.
- o Diverticulosis can cause fistula formation, haemorrhage,
intestinal obstruction, peritonitis, etc.
- o In fistula formation, commonest type is vesicocolic which
leads to pneumaturia or faeces in urine
- o Diverticula of colon are acquired herniation of colonic
mucosa protruding through circular muscle coat at the
points where blood vessels penetrate the colonic wall.
Increased segmentation and intraluminal pressure
- o Saint's Triad --- diverticulosis, gall stones and hiatus
hernia
- o Right sided diverticula are more common than left sided
- o Low fibre diet predisposes to diverticula formation
- o T/t:

In acute cases of diverticulitis, flexible sigmoidoscopy
or colonoscopy is contraindicated d/to risk of colonic
perforation however, later it may be very useful

If there is obstruction, perforation, oedema, adhesions, then
Hartmann's procedure is operation of choice

In elective cases, resection and primary anastomosis is
done.

- o Hinchey classification is used to describe perforations of
the colon d/to diverticulitis.

Ischemic Colitis

- o M/c site --- Splenic flexure.
- o M/c form of GI ischemia.
- o Occlusive obstruction is m/c caused by embolus or
thrombosis in SMA/IMA.
- o D/g is confirmed by colonoscopy (Most sensitive &
specific).
- o Presentation : abdominal discomfort & bloody diarrhoea
seen in elderly, debilitated persons.
- o Thumbprinting/pseudotumours on air-contrast/barium
contrast enema.
- o Transmural & extensive involvement require surgery (Total/
subtotal colectomy with end ileostomy).

APPENDIX

Appendicitis

- o M/c organism causing appendicitis --- E. coli.
- o Organism causing appendicitis like syndrome ---
Strongyloides stercoralis.
- o IOC in appendicitis --- CECT

- 2.5cm appendicular carcinoid is best treated by ileocecal resection.

Appendicitis in Crohn's d/s patient

- If caecal wall is healthy --- Appendicectomy should be done
- If appendix is involved --- Conservative t/t

C/c of appendicectomy

- Infection is a c/c of open appendicectomy.
- Wound infection is m/c on post-op-day 4-5
- Adhesive intestinal obstruction --- m/c late c/c
- RIOH --- Injury to iliohypogastric nerve

RECTUM

Rectal Prolapse

C/F	Partial	Complete
Prolapse of	Mucosa + submucosa	All 3 layers
Prolapsed length	1-4 cm.	>4 cm
Common in	Extremes of ages infants & elderly	Elderly, females after hysterectomy
A/w	3° piles	Fecal incontinence in >50%
T/t	Goodsall's ligation	-

- Recurrence rates are minimum (3-4%) with rectopexy. Wells and Ripstein repairs are extremely successful.

Hemorrhoids

- External piles/false piles occur below the pectinate line and are therefore, very painful. They do not bleed on straining at stool.
- Internal piles/true piles/ 1^0 piles are saccular dilatations of the internal rectal venous plexus. They occur above the pectinate lines & are, therefore painless.
- Primary hemorrhoids are located at rectal position 3, 7 & 11 o'clock which are the m/c site of internal piles (related to branches of superior hemorrhoidal veins when viewed in lithotomy position).
- Secondary (2^0) hemorrhoids usually occurs b/n the primary sites - 8, 9, 10, 1 & 4 O'clock positions.
- Bleeding is the first symptom (splash in the pan).

C/F and T/t

Degree	C/F	T/t is
1^0	Bleed but do not prolapse.	Conservative, Sitz baths
2^0	Prolapse but return back spontaneously or by digital reposition	Sclerosing Barron's banding
3^0	Permanently prolapsed	Hemorrhoidectomy

- Surgery is indicated for
 - 3^0 piles
 - 2^0 piles not cured by non-operative methods
 - fibrosed piles
 - interioexternal piles

→ An arterial pile — hemangiomatous condition of superior rectal artery; an internal pile

Fistula-in-ano

- Is a track, lined by granulation tissue, that connects deeply in the anal canal/rectum and superficially on the skin around the anus.
- Classified into high or low depending on whether the track passes above or below the anorectal ring. High level fistulae open into the anal canal at or above the anorectal ring (internal ring).
- Goodsall's rule**
Fistulas with an external opening in relation to the anterior half of anus (within 1.5 inches) is of direct type. While fistulas with external opening in relation to posterior half of anus has a curved track (more common variety) may be of horseshoe type, opens in middle posteriorly.
- Classification

Standard	Park's classification
Subcutaneous (commonest)	Intersphincteric (commonest)
Submucous	Supralevator
High anal	Anal
Low anal	
Pelvirectal	

- Rectal continence depends solely on the anorectal ring.
- Low level fistula can be laid open with less risk of permanent incontinence, while high-fistula can be treated only by 'staged' operations.
- M/c symptom is persistent seropurulent discharge
- T/t: Low fistula (fistulectomy)
High fistula (initial colostomy later closure)

→ Anal fissure is best diagnosed --- clinically by history and visual inspection

LIVER & GB

Plate system of liver

- **Capsular plate system** of liver consists of bile ducts and blood vessels surrounded by a sheath. There are 3 plates in the hilar area: the hilar plate, the cystic plate, and the umbilical plate.
- **Ductal plate** is a primitive biliary epithelium. It develops from periportal hepatoblasts. Malformations of ductal plates can result in:
 1. Interlobular bile ducts ---- ARPKDs
 2. Smaller interlobular ducts --- Von Meyenberg complexes.
 3. Larger interlobular ducts --- Caroli's d/s
- **Pringle maneuver** is used to control hepatic bleeding (from hepatic vein and portal artery).

Biliary Cirrhosis

Primary biliary cirrhosis (PBC)	Secondary BC	Prim. sclerosing cholangitis
M/c symptom --- pruritus		A/w IBD (50-70%), HIV
Common in females	No sex predilection	More in males
Auto-immune (Anti-mitochondrial Ab+nt)	Conjugated hyperbilirubinemia ↑serum ALP, cholesterol	<u>Auto-antibodies to colonic & ductular epithelium</u>
Lab/F - ↑ serum ALP, IgM		Lab/F ↑ IgM, ↑ Ig
Periportal fibrosis , clubbing hepato/splenomegaly, xanthelasma	Past H/O Gallstone, biliary tract surgery	Periductal fibrosis, segmental stenosis of EHB ducts.
Mallory bodies + nt	Centrilobular bile stasis bile lakes, cholangitis.	

Acute bacterial cholangitis

- Active infection of the biliary tree (acute ascending cholangitis).
- Symptoms are referred as **Charcot's triad**: RUQ pain (biliary colic) + jaundice + fever with chills.
- Illness may progress rapidly with septicemia and disorientation, k/as *Reynold's pentad* i.e. RUQ pain + jaundice + fever + septic shock + mental state changes.
- M/c organism are Gram -ve enteric bacilli.

→ **Charcot's triad** is also seen in multiple sclerosis which is nystagmus + intention tremors + dysarthria.

Obstructive/ Sx Jaundice

- M/c cause - stones in GB.
- M/c site of impaction of stone in GB Ampulla of Vater.
- Symptomatic retained gall stone is treated by - Sphincterectomy/ESWL/Lap.

CBD Stones (Choledocholithiasis)

- **CBD stone** causing obstruction produces future infection with ascaris lumbricoides or Clonorchis sinensis.
- **Courvoisier's law**
In a case of obstructive jaundice if GB is palpable, it is seldom d/to choledocholithiasis (CBD stone). Organ is usually shriveled d/to repeated attacks of inflammation and fibrosis.

Exceptions to Courvoisier's law

- Double impacted stone; at CBD and cystic duct
- Periampullary carcinoma or Ca head of pancreas
- Past h/o cholecystectomy

- M/m ---

Endoscopic papillotomy is the preferred first technique with sphincterotomy removal of the stones using a Dormia basket or placement of stent if stones are not removed.

- Endoscopic sphincterectomy is unlikely to be successful in patients with large stones e.g. (> 2 cm) and it is contraindicated in presence of stenosis of bile duct proximal to the sphincter. large stones are treated by cholecystectomy + T tube
- If technique fails than percutaneous transhepatic cholangiography can be used to provide drainage and subsequently percutaneous choledochoscopy is done.
- First investigation in a biliary tract disorder- USG

Acute calculous cholecystitis /Gall stones

- Acute inflammation of the GB. Pain is m/c symptom.
- 2° to the obstruction of the cystic duct, which is nearly always d/to a gallstone /cholelithiasis (in 95% cases).
- C/F: Usually acute and severe RUQ pain. Severe abdominal pain lasting >7 days may be the result of empyema of GB. Gallstone ileus may result.
- Rx: Interval cholecystectomy.

Asymptomatic Gall Stones are seen in :-

1. Diabetics.
2. Size <3cm
3. Typhoid carriers
4. Pregnancy
5. GB polyp >1 cm.
6. Multiple small stones with wide cystic duct.
7. Porcelain GB

Indications of cholecystectomy in Gall Stones:-

1. In patient who are symptomatic.
2. Younger patient at risk of malignancy
It is wise to operate younger patient to temporize in elderly.
4. Gall stones d/to S.typhi infection
5. Large gall bladder polyp (> 2 cm) may be a/w abscess. So it should be removed by cholecystectomy.

- Avoid cholecystectomy in patient with asymptomatic gallstone and elderly
- Magnetic Resonance cholangiopancreatography (MRCP) is the gold standard Ix for evaluating biliary tree.

Gall stone ileus

- Gallstone ileus results from impaction of stone in small bowel at some point usually at ileocecal valve in the distal ileum.
- *Rigler's triad* is seen :
Pneumobilia (Air in biliary tree) +
Small bowel obstruction (Multiple air fluid levels / Radio-opaque shadow in intestine) +
Gall stone, usually in the RIF..
- T/t : Exploratory laparotomy + removal of stones.

Bouveret Syndrome

- Stone stuck in duodenum leads to → gastric outlet obstruction.

Emphysematous Cholecystitis

- M/c pathogen: **Clostridium**. E.coli is 2nd m/c organism.
- Immediate cholecystectomy is required.

Acalculous Cholecystitis

- About 20% of cases of acute cholecystitis occur in the absence of stones (acalculous cholecystitis).
- It mainly results from cystic obstruction by another process e.g. malignant tumour, rarely it results from

cystic artery occlusion or primary bacterial infection (by E.coli, clostridium, salmonella).

- Common in hospitalized trauma victim & in patient receiving TPN, burn pt. etc.
- Small vessel occlusion occurs early & if untreated results in gangrenous cholecystitis & complications
- D/g by HIDA scan
- T/t: Cholecystectomy .

CBD Injury

- Common in fundus part
- In Lap- cholecystectomy --- Upper CBD injury is common
- 15% detected intraoperatively while majority of injuries (85%) afterward.

M/m of Post Lap -chole bile leakage

- Patient presents on post-op day 2 with bile output <100 mL/d ---- T/t is Observation
- Patient presents on post-op day 7 with bile output >100-150 mL/d ---- T/t is ERCP
- Patient presents after post-op day 10 with biliary collection on USG ---- Biliary drainage should be done.

- *Strawberry GB (Cholesterosis)* is diffuse deposition of cholesterol-esters in the lamina propria of GB wall. GB mucosa is brick red & speckled. Predisposes to cholesterol stones in GB.

- *Porcelain GB* is calcification of GB d/to stones in GB.

- *Hemobilia* is d/to hepatic trauma → bleeding from intrahepatic br. of hepatic artery. T/t is blood clot infusion in hepatic a. Triad of clinical features of malena + obstructive jaundice + biliary colic (RUQ pain) is k/as **Hemobilia triad** (*Sandblom/ Quinke's triad*)

LIVER TRANSPLANTATION

- Most transplant livers come from a donor who has recently died (cadaver).
- M/c indication in adults is cirrhosis.
- M/c indication in children is biliary atresia.
- Pediatric patient usually receive a segment of liver from adults (partial liver transplantation). The donor's liver soon grows back to normal size after the surgery, while the segment of the liver that was transplanted also grows to normal size.
- 80-85% of liver transplants are successful.

Choledochal cyst

Refer : Pediatric Sx section

HYDATID CYST OF LIVER

- Hydatid cyst of liver has 3 layers
 1. Adventitia (pseudocyst)
 2. Laminated membrane (ectocyst)
 3. Germinal epithelium is only living part lining the cyst (endocyst) → Secretes hydatid fluid, brood corpuscles with scolices.
- **Hydatid fluid** is clear sterile fluid with high specific gravity (1.005 – 1.009), shows hooklets and scolices, antigenic proteins.
- **Pathogenesis**
 - Infection is acquired by grass/ vegetables contaminated with dog feces containing larval cyst of *E. granulosus*.
 - I/H man, sheep; D/H -- dog
- Cysts may occur in liver (**m/c** site in adults), lung (**m/c** site in children), brain, spleen, mesentery etc.
- **CI/t:**
Usually asymptomatic, palpable liver with classical thrill (hydatid thrill) elicited by three finger test
- **Investigations**
 - *USG* is diagnostic (*multiloculated cyst on USG*)
 - *Water Lilly* sign d/to lung cysts is seen on CXR
 - Serology → IHA test & ELSIA are most specific
 - *Casoni's test* (*intradermal skin test*)
- **C/c**
 - Rupture into biliary channels is commonest → resulting in obstructive jaundice or acute cholangitis (cf. with amoebic cyst of liver which most commonly ruptures into lung).
 - When ruptures into peritoneal cavity → causes anaphylactic reaction, shock & even death
- **T/t**
(When excision is planned) After laparotomy fluid from cyst is aspirated cautiously & cyst cavity is injected with **scolicidal agent** (e.g. *certimide*, *chlorhexidine*, *heperton saline*, H_2O , *sodium hypochloride*). Formalin is not used
In case with biliary communication only hypertonic saline is used.

Laparoscopic pericystectomy is done in which cyst is separated b/n adventitia & laminated membrane (ectocyst) which can be easily peeled off. Pericyst (Adventitia) is formed d/ to reaction of host's tissue (liver) to the parasite & is inseparable. PAIR (Percutaneous aspiration - instillation-reaspiration) procedure is also used to drain hydatid cyst.

→ *Malignant hydatid d/s is caused by echinococcus multilocularis (Alveolaris) which is a benign d/s & presents with multiple small cyst in both lobes of liver, all over.*

PYOGENIC LIVER ABSCESS

- Liver abscesses are m/c intra-abdominal abscess
- **M/c cause** --- Enteric gram negative organism (*E.coli*) from biliary tract, staph from hematogenous route.
- Jaundice is m/c feature.

AMOEBIC LIVER ABSCESS

- Almost always a complication of amoebic dysentery (usually an ascending infection).
- Jaundice is least/c feature.
- C/F: Pain, fever, jaundice.
- **M/c primary site** is --- Paracaecal region of liver
- **Anchovy sauce pus** is characteristic.
- IHA is +ve in 90-95% of patients
- May rupture in pleural cavity, results in **anchovy sauce appearance** of pleural fluid.
- Medical t/t : Metronidazole in dose of 800 mg TDS x 10 days.
- Indications of Sx :
 - Size >5 cm
 - Rupture or impending rupture
 - Refractory to medical t/t (after 4-5 days).
 - Pregnancy, diabetes, immunocompromised state.
 - Left lobe abscess.

PANCREAS

ACUTE PANCREATITIS

- **M/c cause** --- gall stones (cholelithiasis). Other imp causes are alcoholism, hypertriglyceridemia, DM, ERCP
- **Mechanism** --- autodigestion. Activation of proteolytic enzymes esp trypsin and phospholipases are responsible
- **M/c symptom** --- abdominal pain in epigastrium and radiates to back

- O/e there is low grade fever, tachycardia, hypotension. **Cullen's sign** (periumbilical light bluish discoloration d/ to hemoperitoneum), and **Grey Turner's sign** (dark bluish/greenish discoloration of flanks) may be seen
- Most important screening test --- serum amylase. >3 fold rise in amylase levels clinch the d/g if other causes of hyperamylasemia e.g. salivary gland d/s or gut perforation are excluded. Serum amylase may return to normal in 3-4 days but **lipase** values remain elevated for 7-14 days (s. lipase is more specific)
- Atlanta classification is used for acute pancreatitis.
- 3 type of scoring is used for acute pancreatitis.
 1. Ranson's criteria in acute pancreatitis include:
 1. Age >55
 2. Blood sugar >200
 3. AST or SGOT > 250
 4. LDH > 400
 5. TLC > 16,000
 2. APACHE : Bed side scoring of severity.
 3. **Balthazar score** is CT severity index used in acute pancreatitis.
- **Lab/f** : Leucocytosis, *hyperglycemia*, *hypocalcemia*, hyperbilirubinemia, very high LDH, hypertriglyceridemia
- **D/g** : CT confirms d/g

- *Biliary tract stones are m/c cause of acute pancreatitis while alcoholism is m/c cause of chronic pancreatitis.*
- *Sausage pancreas is d/to biliary & pancreatic duct strictures seen on CT in autoimmune pancreatitis.*

Pseudopancreatic cyst

- **M/c cause** --- 1 to 4 weeks after acute pancreatitis (but **trauma** is **m/c cause** in children)
- **M/c site of origin** --- 85% in body / tail of pancreas
- **M/c Location** --- Lesser sac (between colon and stomach)
- P~ do not have epithelial lining [false epithelium]
- Presents with abdominal pain usually a/w raised enzymes s. amylase
- **D/g** : USG is IOC . CT-scan is more sensitive & specific than USG
- **R_x** :
 - May regress spontaneously if size <5cm
 - If > 5-6 cm in diameter and >6 wks duration i.e. formed cyst → drainage & then gastrojejunostomy/ cystojejunostomy
- **C/c-Infections** (14%), intracystic hemorrhage [6%], rupture [7%] calcification in cyst wall is rare

- **M/c cause of death** → hemorrhage / rupture.
- For cyst arising during chronic pancreatitis surgery is TOC. external drainage is preferred if cyst wall is not sufficiently thick to allow anastomosis with gut.

Annular Pancreas

- Presence of a band of normal pancreatic tissue that partially or completely encircles the IInd part of duodenum.
- Usually results from failure of normal clockwise rotation of ventral pancreas, or from expansion of ectopic pancreatic tissues.
- TOC is duodenojejunostomy.

- *M/c site of ectopic pancreatic tissue - stomach.*
- *M/c site of ectopic spleen tissue - hilum.*
- *M/c site of ectopic gastric tissue - appendix.*

SPLEEN

Splenic trauma

- Spleen is the m/c organ injured in blunt trauma abdomen
- Mortality increased with blunt injury more than penetrating
- Trauma is the m/c common indication for splenectomy
- Splenic sepsis is more common in children
- Abdominal CT is specific in diagnosing solid organ injury.
- **Balance's sign**-- Dullness in LUQ d/to subcapsular collection of blood in blunt trauma abdomen.
- In children if CT-scan defines the damage limited to parenchymal rupture only, TOC is observation for 7-14 days but if injury to the other abdominal organ present / Hilus is injured/extensive bleeding → do splenectomy
- **FAST** ultrasound (Focus Abdomen Sonogram for Trauma patient) should be done in all trauma patients. It includes a quick assesment of pericardium, pleural space, liver, spleen and Morrison's pouch
- **Conservative t/t** is advised --if there is partial tear, small subcapsular tear, patient is hemodynamically stable
- **Splenectomy is advised** --- For **hilar** injuries, pulverized splenic parenchyma, grade 2 or + injury in a pt of coagulopathy

- Splenic artery embolization is indicated --Grade III laceration, contrast leak in CECT (bleeding patient).
- Ideal time for platelet transfusion during splenectomy --- after ligation of splenic vessels.

Absolute indication for splenectomy

- HS (Hereditary Spherocytosis)
 - Trauma [most common indication]
 - Bleeding esophageal varices with splenic vein thrombosis
 - Splenic abscess, echinococcal cyst, primary splenic tumors
 - Spontaneous rupture
- Sickle cell ds is m/c cause of autosplenectomy.
- Massive splenomegaly is seen in--- HCL, CML, Kalazar, malaria, myelofibrosis, portal hypertension.
- CML is the m/c cause of massive splenomegaly.
- In India splenectomy is most commonly performed for trauma
- Hydatid cyst is the m/c cause of splenic cyst.
- M/c infection after splenectomy--- Streptococcus pneumoniae.
- Vaccines advocated in patients undergoing splenectomy--- Pneumococcal, meningococcal & H. influenzae.

C/c after splenectomy

- Atelectasis of left lower lobe of lung is the m/c complication after splenectomy
- Acute gastric dilatation, delayed perforation, subphrenic abscess.
- Injury to tail of pancreas results in post-operative pancreatitis, pancreatic fistula, abscess, or phlegmon
- Infections after splenectomy in descending order
Pneumococcus > E.Coli > H. influenzae > meningococci > staph > strepto
- Hematological changes after splenectomy
 1. Thrombocytosis is the first and m/c change after splenectomy. Platelets start rising within few hours after splenectomy because sequestered platelets are released in systemic circulation. Transient leucocytosis may be observed. ↑Viscosity of blood
 2. RBCs life span is unchanged & Hb is not affected.
 3. Howell-jolly bodies [nuclear remnants in circulating erythrocytes] persist for many years.
 4. Target cells, reticulocytosis.

Splenic rupture

- M/c cause --- trauma
 - Malaria is m/c cause of spontaneous rupture of spleen. (IM is common cause in western world)
- During 5th - 8th months of fetal life spleen is active in production of both RBCs & WBCs. Spleen is involved in only platelet entrapment in adult life.

Accessory spleens or spleniculi

- In the derivatives of the dorsal mesogastrium i.e. gastrosplenic ligament, lienorenal ligament, gastrophrenic ligament and greater omentum.
- In the broad ligament of uterus
- In the spermatic cord.
- At hilum of the spleen, along the splenic artery, within the pancreas.

Asplenia

- Absence of spleen.
- In an asplenic person dog bite can lead to severe/fatal infection with capnocytophaga canimorsus.

HERINA

- Richter's
If the content of hernial sac is a portion of the Circumference of the intestine It usually complicates femoral hernia. A/w gangrene and perforation. [remember Cir is involve in Ric]
- Littre's
Content of the hernial sac is the Meckel's diverticulum.
- Sliding
Common on left side. Seen exclusively in elderly males. Contains sigmoid colon & its mesentery on the left & caecum on the right side also called Hernia-en-glissade. Truss are c/ind in elderly pt.
- Maydl's hernia :
A loop of bowel in form of 'w' lies in hernial sac and the centre of the 'w' loop is strangulated. Strangulated loop the 'w' lies within the abdomen, thus local tenderness is not marked.
- Spigelian :
Interparietal hernia occurring at level of arcuate line.

o **Epigastric :**

Fatty hernia of the linea alba (occurs b/n xiphoid process & umbilicus).

o **Serofini's :**

Hernia occurring behind the femoral vessels.

o **Cloquet hernia** --- hernia through pectineal fascia

o **Sciatic hernia** --- hernia through greater/lesser sciatic foramen

o **Parastomal hernia** --- hernia most commonly seen with end colostomy.

Strangulated Hernia

o In infancy, m/c site is ---femoral and m/c content is ovary

o Gangrene develops within 6 hours of strangulation.

o Gangrene develops at the ring of constriction at anti-mesenteric border

o Femoral and indirect hernia are more likely to strangulate

o Irreducibility is common in omentocoele

o Femoral hernia is a/w Richter's hernia in which truss are not given. Strangulation is common (40%)

Umbilical Hernia

o Absence of rectal fascia, surgery done >4 yrs

o spontaneous closure may occur

→ M/c of all hernias --- indirect inguinal hernia & m/c hernia in elderly---direct inguinal

→ M/c hernia in females is--- indirect inguinal hernia

→ Indirect inguinal hernia strangulates more commonly than the direct inguinal hernia

→ TRUSS are c/ind in infantile hernia, and sliding hernia

→ TEPP (Total extraperitoneal procedure) is indicated in b/L recurrent inguinal hernia

→ Right sided femoral hernia is more common than left sided one

→ Femoral and indirect hernia is more likely to strangulate.

→ In a patient of femoral hernia, femoral vein would be immediately lateral to the sac of hernia.

o M/c type of hernia is ---Inguinal

o Hernia most likely to strangulate - femoral.

o Pantaloon hernia is m/c overlooked hernia in surgery.

o Varicocoele is more common on left side.

Rectus sheath hematoma

o Earliest sign is bluish discoloration of skin.

o Hypovolemic shock may develop.

o T/t is excision.

Remember

There are 4 type of obstruction for which operation should be done as soon as possible after admission :

- Strangulation
- Closed loop obstruction
- Colonic obstruction
- Early simple mechanical obstruction

There are 2 examples of obstruction that occlude vascular supply as well as intestinal lumen (Strangulation with closed loop obstruction):

- Incarcerated inguinal hernia.
- Volvulus

Rule that constipation is present in intestinal obstruction does not apply in case of

- Richter's hernia
- Gallstone obstruction
- Mesenteric vascular occlusion
- Pelvic abscess associated with obstruction

All hernia that reach the stage of vascular compromise produce local signs & symptoms of intestinal obstruction except:

- Richter's hernia
- Littre's hernia
- Omantocoele

KIDNEY

HYDRONEPHROSIS

o Staging:

Stage I = Dilatation of ureter

Stage II = Dilatation of ureter + Calyx

Stage III = Dilatation of ureter + C + P

Stage IV = Blunting of calyces

o Serial USG monitoring is required in follow up.

Absolute C/Ind to renal transplantation are

- Malignancy
- Severe arteriosclerosis
- Pulmonary disease
- Active hepatitis
- Renal d/s requiring transplantation in descending order DM with renal failure > hypertensive nephropathy > GN
- "Contraindications to renal transplant includes presence of untreated malignancy, HIV infection & chronic infection with hepatitis B"
- Renal transplantation is the TOC for children with end stage renal disease (ESRD).
- Renal transplantation is generally contraindicated in oxalosis because the d/s occur in the transplanted kidney.
- Emotional instability or severe psychosis has been thought to a contraindication to renal transplantation.

Renal conditions & T/t

- Perinephric abscess -- Subcapsular nephrectomy or percutaneous nephrostomy are T/t options
- Hydronephrosis -- Serial USG & if dilatation is increasing then only decompression by nephrostomy
- Pyonephrosis -- Antibiotics + large PC /open nephrectomy
- Renal adenocarcinoma-- Partial nephrectomy
- PCNL (Percutaneous nephrolithotomy) is currently the procedure of choice for removing large and complex renal calculi >2.5 cm, resistant to ESWL, lower pole calyx stones. C/c is bleeding but hydrothorax can occur if done through 11th ICS.

PROSTATE

BPH

- M/c cause of urinary retention in an elderly male.
- M/c site of BPH : Median lobe.

TURP Syndrome

- C/by intravascular fluid volume shift and effects of plasma solutes after TURP
- **Hypo-osmolality** (rather than hyponatremia) is the crucial physiological derangement leading to CNS dysfunction and hypovolemic c/c.
Irrigation with hypotonic fluids → water intoxication → hyponatremia → hypoosmolality → CNS symptom

- If distilled water has been used, severe hemolysis with ARF may occur. Even isotonic fluid like glycine may cause problems by expanding the blood volume, which causes hypertension, and reduces electrolyte concentration, with resultant neuromuscular disturbances such as convulsions & temporary paralysis.
- Acute hyponatremia d/to intravascular absorption of sodium-free irrigating fluids, may cause confusion, agitation, visual disturbances, pulmonary edema, seizures.
- **Intra-operative fluid of choice for irrigation— 1.5% isotonic glycine**
Post-operative fluid of choice for irrigation— 0.9% Normal saline

→ Risk of intravascular hemolysis & hyponatremia is greatly reduced by use of osmotically active irrigating solutions (1.5% isotonic glycine).

BLADDER & URETER

Dietl's crisis

- It is d/to small stone into the ureter which causes u/L obstruction and hydronephrosis. It presents as acute pain & swelling/renal lump. After sometimes as stone passes away pt has diuresis and pain/ swelling subsides (Intermittent hydronephrosis).

Ureterocele

- Cystic enlargement of intramural portion of ureter which probably results from congenital atresia of ureteric orifice. On excretory urogram : Cobra head/adder head app.
- Rx : endoscopic diathermy incision & post operative detection of urinary reflux by MCU.

→ **Golf hole ureter** --- is seen in TB of ureter

→ **Thimble bladder** is seen in ---Tuberculous cystitis, and interstitial cystitis (no increased risk of carcinoma)

→ **Hunner's ulcer** is seen in ---Interstitial cystitis (Painful bladder syndrome).

→ **Teardrop bladder** is seen in --- extraperitoneal rupture of bladder

→ **Kiss cancer of bladder** is seen in --- benign papilloma of bladder

→ **Flooding prostate** is seen in--- membranous urethral injury.

RUPTURE OF BLADDER

Intra-peritoneal	Extra-peritoneal
<ul style="list-style-type: none"> • D/t sudden blow to lower abdomen & pelvis (blunt trauma) particularly <u>with full bladder</u> 	<ul style="list-style-type: none"> • Closely associated with pelvic #
<ul style="list-style-type: none"> • <u>Dome</u> of bladder is weakest & most vulnerable part. 	<ul style="list-style-type: none"> • M/c type of bladder rupture. (80%)
<ul style="list-style-type: none"> • M > F 	<ul style="list-style-type: none"> • M > F
<ul style="list-style-type: none"> • Urine collects in rectovesical pouch. 	<ul style="list-style-type: none"> • Urine spreads in retroperitoneal space. There is transperitoneal extra peritoneal collection of urine. (as in rupture of membranous urethra)
<ul style="list-style-type: none"> • Urine extravasates in peritoneal cavity leading to peritonitis 	
<ul style="list-style-type: none"> • On cystogram Extravasation of contrast outlines loops of bowel & fills the paracolic gutters urine spreads in peri-vesical space) 	<ul style="list-style-type: none"> • On cystogram Extravasation of contrast into pelvis & around the base of bladder (tear drop deformity /
<ul style="list-style-type: none"> • T/t Laparotomy and repair (celiotomy) followed by postop drain by catheter 	<ul style="list-style-type: none"> • T/t: Insertion of Foley's catheter Laparotomy and repair

Displaced anterior pelvic

Rupture of bladder or disruption of membranous urethra is m/c genitourinary injury following displaced anterior pelvic # (15%). Evaluation of suspected genito urinary injury should begin with a retrograde urethrogram prior to insertion of a Foley catheter



If urethra is intact & hematuria is present, evaluation should proceed to cystogram.

Neurogenic bladder

D/t spinal cord lesions above sacral segment. 2 types

- Automatic reflex bladder--- is secondary to damage to afferent limb of micturition reflex.(overflow incontinence)
- Atonic bladder
- Autonomous bladder ---d/t peripheral damage of both motor and sensory pathway.
- Uninhibited neurogenic bladder --- excessive fasciculation
- Over-reactive bladder is seen in --- ?UTI

Urethral Injuries

- Anterior urethra includes bulbar and pendulous, while posterior urethra includes prostatic and membranous part.
- Urethral injury is suspected in patient with blood at meatus, inability to void or penile edema.
- Classic triad in bulbar urethral injury is :
Retention of urine + perineal hematoma + blood from external urethral meatus
- Occur more frequently in males because of the fixity to pubis.
- Urogenital diaphragm is the anatomical landmark that divides anterior (bulbar & pendulous) from posterior (prostatic & membranous) urethral injuries.
- *Traumatic rupture of urethra above the UGD* (rupture of prostatic urethra) leads to extravasation of urine in retroperitoneal space > periprostatic, perirectal spaces (intrapelvic extraperitoneal collection of urine).
- *Traumatic rupture of urethra below the UGD* (rupture of membranous/ bulbous urethra) results in extravasation of urine into the superficial perineal pouch and this urine can spread to scrotum, penis, ant. abdominal wall.
- If the tip/ distal part of penile (spongiosae) urethra ruptures and Buck's fascia is intact, extravasation is limited to penis only.

Anterior urethral injury	Posterior urethral injuries
<ul style="list-style-type: none"> • Usually results from blunt trauma such as a <u>straddle injury</u> (in which the bulbous urethra is crushed against pubic rami) • Scrotal, perineal '<u>butterfly</u>' <u>hematoma</u> seen. 	<ul style="list-style-type: none"> • 90% of P-have simultaneous pelvic #

- *Anterior urethra* includes bulbar and pendulous urethra. while *posterior urethra* includes prostatic and membranous part.
- Watercan perineum is a c/c of recurrent periurethral abscesses after urethral strictures which ruptures on skin. A/w gonococcal infection.

- *M/c type of bladder rupture — Extraperitoneal.*
- *M/c type of bladder rupture a/w pelvic # — Extraperitoneal.*
- *M/c type of urethral injury a/w pelvic # — Membranous*
- *Urethral injury leading to floating prostate — Membranous*
- *M/c type of urethral injuries /rupture — Bulbar*
- *M/c site of gonococcal urethral stricture — Distal bulbar urethra.*
- *M/c cause of acquired urethral stricture — Instrumentation*

Hematuria

- **Initial hematuria** --- In urethral / meatal trauma
 - **Terminal Hematuria** --- Usually arises from the post. urethra, bladder neck or trigone
 - **Total Hematuria** --- Indicates source above UB (Hematuria of renal origin)
 - **Pneumaturia** --- Suggest either a gas producing infection or a fistula (entero-vesical)
 - **Split stream** --- Sign of urethral stricture
 - **Eosinophiluria** --- is seen in antibiotic induced allergic interstitial nephritis, atheroembolic ARF
- *M/c cause of gross total painless hematuria in an elderly male — Ca urinary Bladder*
 - *Sterile pyuria (pyuria without bacteruria) is characteristic of — Genitourinary tuberculosis.*

Incontinence of urine

- **Urge incontinence**
 - M/c type
 - Detrusor instability is the m/c cause in elderly
 - D/g by urodynamic study
- **Stress incontinence**
 - M/c seen in females d/to laxity of pelvic floor (after delivery, prolapse of uterus etc.). Pelvic floor exercises can help in relieving symptoms.
 - **Bonney's test** is done to diagnose it.

Retention of urine

- BPH
- Cauda equina syndrome
- Urethral stricture.

SKIN

Capillary hemangiomas

Salmon-patch (stork - bites or Nevus simplex)

- Present at birth over forehead in midline disappears spontaneously by 1yr.

Strawberry

- Spontaneous remission
- NOT present at birth, appears by 1-3 week
- Natural involution by 7-8 yr.
- Sign of emptying present

Port-wine stain (Nevus flamus)

- Present at birth
- Persistent
- May be a/w Sturge Weber's syndrome

Venous angioma (Cavernous hemangioma)

- Present at birth
- Gradually becomes larger & troublesome
- No tendency of involution

- *Spontaneous remission is seen in strawberry hemangioma & salmon patch. While port-wine stain is persistent.*
- *Congenital AV fistula is an example of arterial hemangioma*

Langer's lines

- Lines of minimal tension in skin running perpendicular to the long axis of underlying muscles
- Obvious on face of elderly
- Incision should be made parallel to the lines on skin i.e. along creases & wrinkles to facilitate healing with minimum scarring. Incision should preferably not be made across the lines & certainly never across flexural creases on flexure surface of joint.

Turban Tumour (Cylindroma of Scalp)

- Rare tumour of scalp skin appendage.
- Locally malignant and slowly growing.

- *Pott's puffy tumour is frontal osteomyelitis.*
- *Cock's peculiar tumour is ulcerated/infected sebaceous cyst.*
- *Acrochordon are m/c mesenchymal tumours. Flesh colored pedunculated lesion over neck, axilla, back, groin.*

SUTURES

- **Absorbable sutures** are --- catgut, chromic catgut, dextron, vicryl and PDS (polydioxone)
- **Non-absorbable sutures** are --- silk, linen, nylon, prolene (polypropylene)
- **Monofilamentous sutures** are --- polypropylene, polyethylene, PDS, catgut, steel
- **Polyfilamentous sutures** are --- polyester, polyamide, vicryl, dextron, silk, cotton

→ Numbering of sutures

2 -- (for pedicle ligation) 2-0 (for bowel suturing)

5-0 (for vascular anastomosis), 9-0 (for ophthalmic surgery (requires operating microscope))

More the no., suture is fine

→ Ideal suture material should have low memory.

→ Isopropyl alcohol is used as preservative while packing sutures. Presterilized by ETO (ethylene oxide).

→ Vicryl is particularly useful in bowel anastomosis (like gastrojejunostomy) and cholecystojejunostomy pancreaticojejunostomy etc.

→ Catgut suture is derived from submucosa of sheep/ cattle gut

BURNS

- Classification and outcomes after burn are based on the **depth** of burn. Classified as partial thickness burns (which heal spontaneously) & full - thickness burns requiring skin grafting.

Class	Depth of burn	Characteristic	T/t and outcome
1 ^o (Superficial)	Epidermis	Erythema	Heals spontaneously without scarring
2 ^o (partial thickness)			
Superficial dermal burn	Epidermis + upper dermis	Blisters	Heals spontaneously /with min ^m scarring
Deep dermal burn	Epidermis + lower dermis		Require excision & grafting
3 ^o (Full thickness)	Destruction of epidermis + dermis	leathray, painless (loss of sensation)	Require excision & grafting, some scarring & loss of func ⁿ
4 ^o (Deep)	Skeletal m/s, fascia, bone		Complete excision, limited function

- Survival after burn depends on the patient's **age & percentage** of burn.

- A rapid loss of intravascular fluid & proteins occurs through the heat injured capillaries. The volume loss is greatest in first 6-8 hr, with capillary integrity returning towards normal by 36 - 48 hours.

- The inflammatory response is cytokine mediated. Secretion of stress hormones i.e. catecholamines (E & NE), cortisol, glucagons, renin-angiotensin, and ADH is increased.

- A profound hypermetabolism & BMR occurs in post burn period owing to ↑ catecholamines & ↑ evaporative heat loss. ↑ ed energy demand is supplied by glycogenolysis & anaerobic glycolysis.

- **Hyperkalemic metabolic acidosis** is seen.

- In burns bulla formation damages the basal cells & basement membrane (subepidermal bulla)

- The total BSA burned is calculated using the **rule of nine** (Rule of Wallace) in adults.

- **Systemic effects of burn**

↓ cardiac output, systemic hypertension, severe hypoproteinemia d/to leaking of plasma proteins, laryngeal edema

Chemical pneumonitis d/to smoke inhalation

CO poisoning

>10% of burn : O₂ therapy is given

>15% of burn : Circulatory shock

- **T/t**

- Follow **ABC** sequence , ET intubation if the patient is semicomatose, has deep burns to the face & neck, or critically injured.

- RL solution (or Hartman solution) i.v. is fluid of choice for infusion in burn pt. *antecubital* vein is preferred (in child tibial marrow infusion might be appropriate). I/v fluid resuscitation is required in burn > 10% in children and > 15% in adults.

- If burns involve > 20% TBSA feeding should be started within 6 hours.

- Best way to relieve pain in burn pt is i.v. morphine (3-5mg)

- Ointments---AgNO₃, silver sulfadiazine (m/c used) , and mafenide acetate (able to penetrate the eschar and particularly useful against resistant pseudomonas & enterococcus species).

- Escharotomy is done in deep 2^o or 3^o burn wounds encompassing circumference of an extremity.

- **Fluid resuscitation**

Parkland formula is used to calculate replacement fluid in

first 24 hours.

Fluid is = 4ml / % of burn/ kg / 24 hours.

1/2 of this is given in first 8 hours, rest in next 16 hours.

In first 24 hours only crystalloids are given, after 24 hours colloid should be given to compensate plasma loss. Blood transfusion is considered in later (>48 hr) period.

- **Grafting** : full-thickness skin graft (that includes entire dermal + epidermal layer) provides the best outcome in wound coverage, diminishes contracture & provides better cosmetic appearance than STG
- Presence of β -hemolytic streptococci is an absolute contraindication to skin grafting, whereas pseudomonas and staphylococcus are relative contraindications.

→ The m/c cause of first – degree burns are over exposure to sunlight & brief scalding

→ Pseudomonas is the m/c opportunistic bacterial pathogen recovered from burn wounds.

→ Candida is the m/c non-bacterial opportunistic pathogen recovered from burn wound

STONES

Gallstones

Cholesterol	Mixed (90%)	Pigment
<ul style="list-style-type: none"> • Made up of cholesterol solitaire • <u>Solitary</u> • Plae yellow • Associated with cholesterosis/strawberry GB 	<ul style="list-style-type: none"> • Cholesterol + calcium PO_4 / CO_3 + Proteins • Multiple • Multi - faceted • A/w chronic cholecystitis • Cholecystitis 	<ul style="list-style-type: none"> • Ca - bilirubinate • Multiple • Jet black, <u>mullberry shape</u> • No change in GB • formed in hemolytic anemia

- Gall stones are c/c of Caroli's d/s.
- Complication of gall stones are : Acute pancreatitis, cholangiocarcinoma.

→ In sickle cell disease there is high incidence of gall stones but not of renal stones.

→ Urinary stone a/w infections --- phosphate (a/w proteus infection), struvite & matrix stones

→ Stone which is most painful, causes bleeding and have spicules --- oxalate stones.

→ Ca - oxalate monohydrate, Ca-phosphate and cystine stones are NOT fragmented by lithotripsy (ECSWL)

Renal Stones

Stone type	Morpho	Cause/etio	Other/F
Ca-oxalate M/c (75%)	Irregular in shape, sharp projections/spicules +nt ↓ Bleeding, pain	Seen after ileal resection/IBD, Hypercalciuria, hyperoxaluria predispose.	Bipyramidal biconcave
Struvite	Staghorn calculi composed of Ca-NH ₄ -Mg phosphate, coffin lid appearance, Rectangular prism	Formed in alkaline urine, Infection (UTI, proteus) promotes stone formation,	Radio-opaque
Uric acid	Teardrop shape, Flat square plates,	Formed in acidic urine	Radio-lucent
Cysteine		Formed in acidic urine	Flat hexagonal

- IOC for renal stones --- plain X ray KUB.
- IOC for ureteric stones --- NCCT.
- In children with suspected renal tract calculi IOC is US (KUB region)
- 90% of renal calculi are **radio-opaque** (calcium, cystine), while only 10% gallstones are radio-opaque.
- Renal stones which are **radiolucent**
Orotic acid, xanthine, uric acid, matrix, drug stones (Indinavir, triamterene)
Excretory urography is useful to locate radiolucent calculi.

- Stones resistant to ESWL/
Lithotripsy (ESWL) is not effective in--- fragmenting cystine stones. C/ind to lithotripsy are pregnancy, aneurysm of renal artery, bleeding diathesis, cystine stones
- Risk of both gallstones (cholesterol type) & renal (oxalate) stones increases in ileal resection. D/to impaired enterohepatic circulation bile salts are not reabsorbed to saturate cholesterol leading to ↑ cholesterol gall stones

Ureteric (urinary) stones

- The presence of stone passing down the ureter often leads to intermittent attacks of **ureteric colic**
- Almost every attack of colic is a/w microscopic hematuria.
- Pain is leading symptom in 75% of people with urinary stone.

5 sites of anatomical narrowing where stone may be arrested

- Ureteropelvic junction
- Crossing of iliac artery
- Juxtaposition of vas deferens or broad ligament
- The bladder wall (entrance)
- Ureteric orifice

Radiation of pain suggests site of calculi

- Tip of penis (strangury) → stone at intramural part
- Groin, thigh and external genitalia → lower third of ureter
- Pain in loin radiating to groin → upper ureter
- Renal angle or anteriorly hypochondrium → renal stone

TRIAD

- Saint's triad**
- Colonic diverticulosis,
 - Hiatus hernia
 - Gall stones
- [mnemonic CGH-S]

- Beck's triad**
- Present in acute cardiac tamponade
- Hypotension
 - distended neck veins (↑ JVP)
 - muffled heart sounds
- [mnemonic: MDH]

- Cushing's triad**
- ↑ ICT
 - ↑ HTN (systemic hypertension)
 - ↓ RR & HR (slowing of HR & RR)

- Hemobilia triad**
- Malena
 - Obstructive jaundice
 - Biliary colic (RUQ Pain)
- (Sandblom/
Quinke's triad)

Mnemonic mob

(Hemobilia is usually d/to hepatic trauma with bleeding from intrahepatic br. of hepatic artery. t/t of hemobilia is blood clot infusion in hepatic a.)

- Charcoat's triad**
- Seen in CBD stones & indicate acute cholangitis
- Pain + obst. jaundice + fever & rigors

- Meckler's triad**
- In esophageal rupture
 - 1. Vomiting
 - 2. Lower chest pain
 - 3. Cervical s/c emphysema

- Whipple's triad**
- Three essential features of insulin producing tumors (insulinoma) -
 - 1. Spontaneous hypoglycemia
 - 2. CNS / Vasomotor symptoms
 - 3. Relief of symptoms on IV / oral glucose.

- Virchow's triad**
- Three factors predisposing to vascular thrombosis
 - 1. Changes in vessel wall
 - 2. Change in local blood flow
 - 3. Change in blood constituents

- Virchow's nodes**
- Also k/as scalene / signal nodes
 - Are enlarged left supraclavicular LN that drain the abdominal cavity.
- Often the first sign of malignancy of abdomen [stomach adenocarcinoma (m/c) & Ca pancreas, Ca colon, Ca testis].

- **Borchadt's Triad**
- Seen in gastric volvulus
- Acute epigastric pain
 - Vomiting
 - Inability to pass nasogastric tube

- **Murphy's triad**
- Seen in acute appendicitis
- Pain in RIF
 - Vomiting
 - Temperature

(Murphy's sign is seen in acute cholecystitis)

- Classic triad of choledochal cyst - Abdominal pain + Jaundice + abdominal mass
- Classic triad of Wilm's tumour - Abdominal mass + Hematuria + Fever
- Classic triad of RCC - Hematuria + flank pain + flank mass
- Callot's triangle - Bounded by inf. surface of liver (superiorly) common hepatic duct (medially) & cystic duct (below). landmark during cholecystectomy. Content is cystic lymph node
- Kocher's maneuver - is performed to permit mobilization of second part of duodenum during Bilroth-I
- Pringle's maneuver - is for hepatic vein & portal artery.

SIGNS

- Troissier's sign** - Enlargement of Virchow's nodes (left supraclavicular LN) in occult gastric carcinoma etc.
- Trousseau's phenomena/ sign** - Carpopedal spasm elicited by occlusion of brachial artery with a BP cuff for 3 minutes. Seen in hypocalcemia (hypoparathyroidism, alkalotic or latent tetany, hypomagnesemia, hypo & hyperkalemia).
- Chovstek's sign** - Contraction of facial m/s (masseter spasm) elicited by tapping the facial n. anterior to ear.
- Trousseau's sign** - Seen in migratory superficial thrombophlebitis (as in pancreatic ca).
- Homan's sign** - Calf tenderness may be exaggerated by passive dorsiflexion of ankle
- Homman's sign** - Mediastinal crunch seen in esophagus rupture.
- Tinel's sign** - Tingling sensation on percussion.
- It indicates partial lesion or beginning of regeneration of a nerve.

NEUROSURGERY

EDH Vs SDH

EDH	SDH
<ul style="list-style-type: none"> • D/t to tear of <u>middle meningeal</u> a. occurs in association with skull # (petrous temporal bone m/c) • Crosses dural attachments but not sutures • <u>Lucid interval</u> seen • Appears hyperdense biconvex on CT • Requires emergency operation in setting without tertiary care facilities (Burr-hole) 	<ul style="list-style-type: none"> • D/t to disruption of bridging veins between cortical surface, dural venous sinuses (as a result of high velocity injury) • Crosses sutures. • Lucid interval is uncommon • Appears crescentic or concavo-convex (sickle shape) on CT. <ul style="list-style-type: none"> - Acute hyperdense, - Subacute isodense, - Chronic hypodense. • Occurs in presence of cerebral atrophy (so more common in alcoholics, elderly) • Gradual deterioration of mental function with fluctuating level of consciousness.

PEDIATRIC SURGERY

Courtesy : Dr. Anand Singh Kushwaha

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Cystic Hygroma

- Also k/as cavernous hemangioma / lymphangioma / hydrocoele of neck.
- Benign cystic swelling, multilocular, multicystic. Never progress into malignancy.
- Results from obstruction of the lymphatic system. Eventually, sequestrations of usually jugular lymphatic sacs, that do not communicate with normal lymphatic system, develop.
- 50-65% appear at birth & 90% by second year of life
- **Location** : M/c in the posterior triangle of the neck (75%) & axilla (20%), other sites are mediastinum, pelvis, retroperitoneum
- It may result in obstructed labor.
- Majority are asymptomatic
- Brilliantly transilluminant, usually multilocular

- Cyst contains clear lymph and is lined by single layer of epithelium /endothelium (i.e. non-stratified)
- T/t of choice is **complete excision (TOC)** or sclerotherapy (Picibanil/ OK- 432, bleomycin intralesionally) for small, unilocular swelling.

Hypospadias

- It is the m/c congenital urethral malformation.
- M/c variety is glandular, which does not require any t/t.
- Hooded prepuce & chordee are seen.
- Ideal age for repair --- After 2 years
Tubularized incision plate (TIP) or Snodgrass urethroplasty is currently TOC for anterior hypospadias.
- Circumcision should be avoided until hypospadias has been repaired. Foreskin may be useful in urethral reconstruction.



Photograph : Hypospadias

Undescended testis (UDT/ Cryptorchidism)

- M/c disorder of sexual differentiation in boys
- B/L in 10-12% cases.
- The testes may be arrested anywhere in the path of its descent. M/c site is **inguinal canal** (while ectopic testes are found in superficial inguinal pouch or perineum).
- Risk of malignancy is 4-10 times higher, m/c tumour developing in UDT is seminoma (65%).
- C/E (Clinical examination) is the most important step in diagnosing UDT.
- In case of impalpable testes, diagnostic laparoscopy is the next step (not the USG abdomen or MRI).
- Surgery is recommended **b/n 6 mo - 1 year** of age. Most testis can be brought down to the scrotum with orchidopexy. Orchidopexy should be done before the age of 12-24 months to reduce the risk of infertility.
(however orchidopexy does not change the risk of cancer of the testis developing).
- Orchiectomy (Gonadectomy) should be considered if the testis are atrophic & intra-abdominal.
- Medical T/t with hCG.
- 100% UDT have a/w inguinal hernia.

- There is definitive ↑ risk of developing malignancy and infertility in U~.
- Orchidopexy does not change the risk of cancer developing but can reduce the risk of infertility.
- Infants with Retractable Testis are not at risk for infertility or malignancy.

Ectopic Testis

- Common sites :
 - SIR (Just above and lateral to SIR is the m/c site)
 - Perineum
 - At the root of penis
 - In the femoral Δ (thigh)
- Testes are fully developed, functionally normal.
- C/c --- More prone to trauma
- T/t --- mobilization and fixation (orchidopexy).

Congenital Hydrocele

- Accumulation of fluid b/w 2 layers of tunica vaginalis of testes.
- Processus vaginalis communicates with the peritoneal cavity.
- T/t: C~ if persists for >2 years herniotomy should be done.
- M/c type : Vaginal hydrocoele.
- Lord's plication and Jaboulay's procedure (in which sac is everted) is obsolete now a days.

Ectopia vesicae (Exostrophy of bladder)

- A/w epispadias; more common in males.
- Best results are seen if UB is closed within 2 days after birth because once metaplasia develops, its difficult to achieve its function

Gonadectomy is advised in-

- Mixed/pure gonadal dysgenesis (with y chromosome+)
- Gonadoblastoma (In +nce of y chromosome)
- Intra abdominal testes, testicular tumour (orchidectomy via inguinal route)
- True hermaphroditism, Streak gonads

Gonadectomy is NOT advised in incomplete testicular feminization (Androgen insensitivity syndrome). Removal of gonads should wait until after puberty & development of secondary sexual characters, gonads then can be removed around 21 yr. of age.)

PUJ obstruction (PUJO)

- M/c cause of hydronephrosis in pediatric patients
- M/c cause of PUJO is intramural abnormal distribution of collagen
- IOC : DTPA (detects drain or level of obstruction/ renal flow and perfusion)
- Ideal age of repair --- Anderson Hyens pyeloplasty b/w 6-12 months.

VESICoureTERIC REFLUX (VUR)

- Incompetent VUJ d/to shortening and a lack of obliquity of submucosal and intra vesical segments results in VUR
- Genetic basis – AD
- A/w other anomalies e.g. megacystis, megaureter, duplex systems, hydronephrosis, PUV and ectopic ureter etc.
- Secondary VUR is seen in neuropathic bladder, PUV, trauma
- 40% of children/ infant with UTI have VUR. Gross VUR during infancy is seen mostly in boys and is B/L
- Upto 20-40% of children with UTI and VUR develop renal scarring secondary to parenchymal infection, of which 5-10% progress to ESRD. Renal scarring in VUR is best detected by DMSA scan.
- 30% of children have only non-refluxing papillae, and thus protected from intrarenal reflux and scarring. Risk of scarring is highest in your children.
- D/g : MCU or VCUG
- Most sensitive investigation for detection of scarring in children with VUR is radionuclide imaging, particularly DMSA scanning. DRCG was a simple and sensitive technique for identification of reflux in VUR. Also owing to its very low radiation dose, it has an important place in the follow up.
- T/t : VUR is initially managed with antibiotic prophylaxis. The prophylaxis is continued till 1 year of age in patients with VUR grades I and II, and till 5 years in those with higher grades of reflux or until it resolves. Children with VUR should be followed up with serial ultrasonography and direct radionuclide cystograms every 2 years, while awaiting resolution. Siblings of patients with VUR should be screened by ultrasonography.
- P/g: Primary VUR tends to resolve by the age of 6-10 years. Resolution rates are 70-90% in grade I-III and 10 to 35% in grade IV-V.
- T/t
Depends upon child's age, grade of reflux, U/Lor B/L involvement, recurrent UTI

Grade I, II, III -- **Antibiotic prophylaxis** to ensure urinary sterilization (low dose cotrimoxazole/ nitrofurantoin)

Grade III -- Surgical repair is needed in 50% patients (those with renal scars)

Grade IV, V -- Surgery is TOC. STINGS (submucosal transurethral injection of teflon/ collagen) is preferred method. >2 failure require open ureteric reimplantation. acc/to Paquinne's rule

-- Length of sub-mucosal tunnel of ureter should be 5 times to the diameter of ureter (5:1 ratio)

Other indications of surgery are

- Breakthrough infection on antibiotic prophylaxis
- Recurrent symptomatic UTI irrespective of grade
- Persistence of reflux till puberty

To prevent VUR, ratio of intravesical length of ureter : diameter of ureter should be at least 5:1.

→ B/L grade IV or V VUR is better treated surgically with ureteric reimplantation.

→ Ideally surgery should be delayed till the age of one year (because intravesical length of ureter increases with age)

→ A MCU to document cessation of reflux is performed 3-6 months after surgery. In surgically treated children USG should be performed at 6 monthly interval for 5 years.

Posterior urethral valve (PUV)

- D/to failure of posterolateral migration of urethrovaginal fold
- M/c type --- type I (Young's classification), which is distal to veru-montenum
- Exclusively affects boys
- Earlier the presentation poorer is the prognosis.
- Ix---MCU or VCUG is the IOC.
- T/t ---
 1. Cystoscopic fulgration of PUV is TOC.
 2. Vesicostomy (If GC is very poor, KFT is very high and there is b/L high grade VUR).

Meconium ileus

- Earliest clinical manifestation of cystic fibrosis (CF) and occurs in 10-20% of CF pts
- Proximal ileum is dilated and packed with tarry meconium, microcolon (unused colon) is present
- Perforation occurs in ~ 50% of patients

- Soap bubble sign or Heuhauser sign on plain X-ray is diagnostic
- Medical m/m with gastrograffin enema is diagnostic as well as therapeutic. Surgery reserved for failed or complicated cases (perforation etc.)



Anorectal malformations (ARM)

- Classification:
ARM located above PC line = High ARM
" b/w PC line and I- point = Intermediate ARM
" below I- point = Low ARM
- In male 2/3rd are high ARM, while 1/3rd are low ARM
In female 1/3rd are high ARM, while 2/3rd are low ARM
- In male rectal end terminates in b/w PC line (pubococcygeal line) and I-point (comma shaped point of ischium). In female anovestibular fistulas are m/c variety (rectal end terminates high /above PC line in **invertogram**).
- Urogenital anomaly is the m/c associated anomaly ~ in 50% cases.
- T/t
Low ARM / Anal atresia in male --- Y- V anoplasty ,
Intermediate/ high ARM in male --- 3 stage procedure
Sigmoid colostomy then → PSARP (Post Sagittal Ano RectoPlasty) then → colostomy closure
AVF in female --- Primary PSARP

NEC (Necrotising Enterocolitis)

- M/c seen in preterm infants
- Risk factors : Birth asphyxia, top feed, goat milk, theophyllines, vitamin E, exchange transfusion
- Bell's stages:
Stage I (Early, suspect) --- refusal to feed, mild ileus on X-ray
Stage II (Confirm) --- severe abdominal distension, pneumatosis intestinalis
Stage III (Advanced) --- septicemia, gross GI bleed,

pneumoperitoneum (football sign)

- Other finding on abdominal X-ray---Gas in portal vein, fixed bowel loops, Ascini's sign.
- In gut perforation, free gas on supine X-ray film is k/as **Wrigler sign**. Bowel wall becomes bright.
- Absolute indication for surgery--- Pneumoperitoneum

Elective Surgical Conditions and recent trends in Optimum timing of their Surgery

Condition	Ideal age
1. Hirschsprung's d/s	1-3 mo (Single stage primary transanal endorectal pullthrough) >10 Kg Swenson's procedure; Older child/ adult : SOAVE operation
2. EHBA	< 2 mo
3. Cleft lip	2-3 mo (or 10 weeks)
4. Tongue tie	6 mo (before eruption of teeth)
5. Undescended testes	< 6 mo (unilateral cases) 6 mo - 1 yr (bilateral cases)
6. PUJ obstruction	6 mo - 1 yr
7. ARM	At birth → Divided high sigmoid colostomy 6mo -1 yr → PSRAP 3 mo after PSRAP → Closure of colostomy
8. Cleft palate	10 -12 mo.
9. Hydrocoele	>2 yrs
10. Hypospadias	>2 yrs
11. Umbilical hernia	>2-3 yr (If defect is >2 cm and persisting after 2 years) Closure of umbilical hernia is the rule rather than exception.

Conclusion

- Soon after birth (or Day 1) --- All intestinal atresias (Esophageal / duo/ ileal etc.), imperforate anus/ rectum, exomphalos minor (but not exomphalos major)
- CDH (congenital diaphragmatic hernia) should be operated soon after birth after physiological stabilization of patient.
- As early as possible in --- Inguinal hernia, exomphalos minor, sacrococcygeal teratoma (rate of malignancy ↑es with the duration) & meningomyelocele (risk of rupture ↑es as the time passes)

ANENCEPHALY

- A/w shoulder dystocia, postmaturity, polyhydramnios (50%)
- M/c presentation face.
- Cerebral hemisphere & cerebellum are usually absent & only residue of brain stem can be identified
- A/w folded ears, CHD, cleft palate in 10-20%, absent fetal adrenal reticularis zone
- Multifactorial etiology (environmental, genetic basis, low SES)
- Recurrences are common (upto 10% if past h/o 2 anencephalic fetuses is there)

CEPHALIC DISORDERS

- *Lissencephaly* means smooth brain, is a rare brain formation disorder caused by defective neuronal migration during the 12th to 24th weeks of fetal life. Results in profound mental retardation and severe seizures.
- *Holoprosencephaly* also k/as **arhinencephaly** is a congenital brain malformation, resulting from incomplete separation of the two hemispheres.
- *Colpocephaly*: there is abnormal enlargement of the occipital horns-the rear portion of the cavities or chambers of the brain.
- *Iniencephaly* is marked by retroflexion of the head and severe spinal defects. Iniencephalic infants are short, with disproportionately large heads.
- *Megalencephaly* may be caused by a disturbance nerve cell proliferation. Males are mainly affected.
- *Schizencephaly* is a form of porencephaly in which the brain's hemispheres are marked by abnormal slits or clefts.

Meningo-myelocele

- M/c type of NTDs.
- M/c location is lumbar L3-L4.



Photograph : Meningomyelocele

- Associations with aqueductal stenosis → hydrocephalus, Arnold-Chiari II, cerebral cortical dysplasia are very common.

→ *Sacroccygeal teratoma has elements from all the 3 germ layers, the endoderm, mesoderm, and ectoderm. Increased risk of malignancy is there.*

Meningocele

- Midline protrusion of CSF containing sac without spinal cord element within it.
- Maternal serum AFP is not elevated as it is a closed NTD.
- Before operative treatment nursing is advised in prone. A dressing soaked in normal saline should be applied to protect the coverings.
- Cranial meningocele has excellent prognosis.

Cleft lip and palate

- Defect is d/ to failure of fusion of the nasal process with the maxillary process.
- **Midline cleft lip** (Central Cleft Lip) result from failure of fusion of the two globular processes derived from median nasal process.
- **Lateral cleft lip** are of two types
 1. **U/L cleft-lip** results from failure of fusion of the median nasal processes with maxillary process.
 2. **B/L cleft lip** results from failure of maxillary process to unite with the fused medial nasal processes on both sides.
- Malformation of the first branchial arch
- May be sporadic/genetically determined
- It has polygenic/multifactorial inheritance
- Cleft palate can occur as syndromic malformation a/w chromosomal disorders or aneuploidy --- Pierre Robin, Apert or Patau syndrome (B/L cleft lip and palate), lip pit, cleft lip syndrome (Vander Woude syndrome).
- Often a submucous cleft palate is a/w a bifid or cleft uvula.
- VSD is common association as the fusion of ventricular septum also occurs the same time.
- T/t:
 - Cleft lip is generally corrected around **2 months** of age (Manchester repair).
 - Cleft palate should be corrected before the baby learns to speak.

- According to rule of 10 : A cleft lip is corrected at 10 weeks of age and approximately 10 pounds weight. A cleft palate is corrected at 10 months of age and about 10 kg wt
- M/c birth defect/deformity +nt at birth : clubfoot > cleft lip/palate.

Tracheoesophageal fistula (TEF)

- M/c type is type-C of Gross, in which upper end is a blind segment & a tracheal fistula from the lower esophageal segment. It accounts for 87% of cases.
- Cardiac anomaly is m/c associated anomaly. Also a/w polyhydramnios, Down syndrome, single umbilical a., & VACTERAL anomaly.
- Presentation : Drooling of saliva since birth is the symptom. Excessive frothing & choking/cyanosis occurs with first feed.
- Incidence 1:7000
- Males are affected more.
- Put an infant feeding tube at 10 cm and take radiograph. Coiling of tube is s/o TEF. Only in H type tube may go to stomach..

Type	Clinically	Characteristic on passing NGT	T/t and outcome
C type (85%, commonest)	Upper end blind	NGT tip coiled with gas in abdomen (distal E connects to trachea)	Thoracotomy + end to end esophageal anastomosis (Kamron Haight)
A type (Pure atresia)	Both end blind	NGT tip coiled with gasless abdomen	Esophagostomy + gastrostomy

Idiopathic Hypertrophic Pyloric Stenosis (IHPS)

- NEVER congenital
- M/c cause of gastric outlet obstruction.
- More common in first born males and in offspring of a parent with CHPS (familial).
- Associations :
With B & O blood group, high prostaglandins level (can occur in babies who are given PGs to maintain patency of PDA), Trisomy 18, Turner's, Smith Lemli Opitz syndrome, Cornelia de Lange syndrome, Tracheo esoph. fistula.
- Manifestations :
3 'P' which are Palpable tumour in mid epigastrium, Peristalsis visible, Projectile non-bilious vomiting b/w 3-6 week of life (range 1-20 wk).
Other cl/f : dehydration, constipation, jaundice (partial

intestinal obstruction)

- Lab/F : Persistent vomiting leads to dehydration, loss of Cl- and K+ leading to **hypokalemic, hypochloremic metabolic alkalosis with hyponatremia**. But urine is acidic (**paradoxical aciduria**)
- D/g --- Clinical d/g is most important.
USG is IOC (which reveals pyloric m/s thickness > 4mm and pyloric canal length >16 mm)
- T/t - Correction of dehydration using I.V. DNS (0.45% NS + 5% Dextrose + 1 meq/100 ml KCl in a dose of 2-4 meq/kg K+).
- *Ramstedt operation* (pyloromyotomy) is the gold standard.
- Atropine is being tried orally to relax pylorus

Duodenal Atresia

- M/c type of intestinal atresia; common in preterms
- M/c association---30% of DuA are a/w Down's syndrome.
- M/c tsite of congenital duodenal diverticula is - 2nd part of duodenum.
- May be a/w malrotation, esophageal atresia, ano-rectal malformations, CHD, polyhydramnios, Ladd's band, annular pancreas, and duodenal web.
- Cl/f - bilious vomiting, noted on the first day of life with scaphoid abdomen
- Plain X-ray - "Double bubble sign"
- T/t - Kimura's diamond shaped duodenoduodenostomy

Jejuno ileal Atresia

- Apple peel atresia is a variant of ileal atresia.
- T/t is end to oblique anastomosis after resection of atresia.

INTUSSUSCEPTION

- Commonly affects infants at the age of weaning (~ 5-6 months)
- M/c cause of intestinal obstruction in infants.
- M/c variety : ileo-colic.
- Idiopathic is m/c etiology; others are d/to lead point in which MD (Meckel's diverticulum) is m/c.
- Cl/f : "Red current jelly" like stools, with attacks of pain in abdomen, palpable lump with empty RIF (emptying sign) are hallmark.
- On USG : " Pseudokidney" sign or Doughnut sign.
- T/t : USG guided saline infusion and reduction (hydrostatic

reduction) is TOC in uncomplicated case. Laparotomy is indicated if there is gas under diaphragm (intestinal perforation), toxic child (suspected bowel gangrene).

- Single bubble sign is seen in pyloric stenosis/atresia
- Double bubble sign is seen in duodenal obstruction (duodenal atresia, annular pancreas, Ladd's band causing malrotation)
- Triple bubble sign is seen in jejunal / ileal atresia
- All intestinal atresias are a/w polyhydramnios

Ileal atresia

- Apple peel atresia is a variant of ileal atresia
- End to oblique anastomosis after resection of atresia is TOC.

Congenital Diaphragmatic Hernia (CDH)

- Lt. sided hernia is more common
- It is a physiological emergency not a surgical emergency. Neonate's ABG parameters should be stabilized before surgery.
- Approached via transabdominal incision.
- Earlier is the presentation, poorer the prognosis. Gestational age of the neonate at the time of presentation is important but the degree of pulmonary hypertension is the single most important prognostic factor.
- Failure of closure of pleuro-peritoneal membrane is the m/c etiology.
- Malrotation of gut is the m/c association.

Abdominal wall defects: Omphalocele and Gastroschisis

	Omphalocele	Gastroschisis
1. Defect	Central	Rt. to umbilicus
2. Covered with	Amnion, Warton's jelly	No covering
3. A/w	Trisomys, CDH, Cardiac anomalies, EMG syndrome [Exomphalos + macroglossia + gigantism]	Atresia of intestine, LBW
4. Prognosis	Relatively poor	Better
4. T/t	Minor (Small) --- Sx after stabilization Major (Large) --- Wait and watch with L/A of 2% mercurochrome f/b surgery	Primary closure



Photograph: Omphalocele

Malrotation of gut

- Can present at any age
- Malrotation is a surgical emergency in neonates.
- M/c d/to compression of duodenum (IInd + IIIrd part) by Ladd's band leading to partial obstruction.
- C/f: Presents as billious vomiting (compression), scaphoid abdomen (relatively low volume of gas distal to duodenum), FTT.
- Upper GI contrast (barium follow through) is diagnostic. In USS abdomen a SMV is located on the left to SMA.
- There is dilatation of IInd + IIIrd part of duodenum, D-J junction is located rt. to spine, jejunal loop is present on right side of abdomen.
- Malrotation of gut with volvulus (Whirlpool sign).
- T/t: Exploratory laparotomy and correction of malrotation.

Torticollis

- Congenital torticollis is d/to contracture of sternocleidomastoid m/s.
- Physiotherapy is advised.
- Sx t/t is tenotomy. Indications of operation
 - age > 1 yr
 - facial hemihypoplasia
 - plagiocephaly

Torsion Testes

- Acute scrotum in paediatric patient (1 day - 16 yrs) is a torsion until proved otherwise.
- Torsion occurs away from mid line (i.e. Right testes torsion clockwise and left testes torsion anti clockwise)
- Testes are 100% salvagable up to 6 hrs. Delayed the presentation poor is the prognosis.
- T/t
 - Orchiopexy (orchidopexy): Affected testes as well as normal testes should be explored and fixed by non-absorbable sutures if viable.
 - Testes should be removed if non-viable

Rectal Polyp

- Bleeding P/R is the symptom but there is no pain.
- T/t polypectomy

Anal fissure in children

- Pain is the symptom but there is no/minimal bleeding
- T/t : Conservative

Hirschsprung's disease (HD)

- Congenital aganglionic megacolon
- D/ to arrest of craniocaudal migration of neural crest cells (neuroblasts) along vagal trunks before 1st trimester. Probably d/to local deficiency of NO synthetase or abnormal end organ surface receptors.
- Absence of preganglionic parasympathetic ganglia in Meissner's (in muscle) and Auerbach's (submucosal) plexus.
- Aganglionic segment in 80% cases is rectosigmoid, which is short contracted segment
- Familial, M > F, Autosomal Recessive inheritance, a/w Down's syndrome, annular pancreas, TEF. Also a/w RET proto-oncogene
- Presentation :-
Acute intestinal obstruction in neonate, failure to pass meconium in first 24 hrs, chronic constipation, empty rectum on PRE.
- D/g : Suction biopsy > Full thickness formal strip rectal biopsy is IOC
(which shows characteristic aganglionosis with hypertrophied nerve trunk)
Anorectal manometry is a useful screening test which shows -ncc rectosigmoid inhibitory reflex (spikes). Hypothyroidism should be ruled out before labelling it HD.
- Supine X-ray film reveals multiple fluid levels.
"Prone cross table lateral shoot" view is also advised for low ARM or HD.
- Ba-enema --- Rectal examination should not be performed before 2 days.
Finding is --- Collapsed rectum with dilated bowel above it (**coning** or reversal of recto-sigmoid ratio).
Transition zone is absent in ultrashort segment HD & total colonic aganglionosis
Contrast enema identifies meconium d/s and HD so as to avoid surgery and it is also therapeutic for HD as well.
- C/c : Obstruction, NEC, Cecal perforation.
- Severity of symptoms may be related to no. of acetylcholine esterase +ve nerve fibres.
- Definitive operation - Duhamel's pull through operation.

- Colostomy at ganglionic segment- when child present late (e.g. > 4-6 mth.)
- Single stage endorectal pull through - < 4 mth.



TCA Total colonic aganglionosis, (Long segment d/s)

- Variant of HD which constitute ~ 3-12% of HD cases.
- Family history is positive in ~ 33%.
- A/w more complications like enterocolitis etc.
- A/w Wardenberg syndrome.
- 'Saw tooth sign' of sigmoid colon on Barium -X-ray.

Treatment of HD

Diseases	Treatment
Ultra short segment Anorectal Achlasia	Myomectomy
Short segment (Rectosigmoid)	Duhamel's pull through
TCA (long segment)	Ileostomy followed by Martin modification of Duhamel's

Microcolon is seen in

- Meconium ileus
- Ileal atresia
- Total colonic aganglionosis (Mnemonic = Mic)

Choledochal Cyst

- Type I is the most common. There is fusiform dilatation of EHB duct.
- Type V is *Caroli's d/s*. Single or multiple **intrahepatic** cysts are present. A/w pancreatitis. **Central dot sign** +nt.
- D/to anomalous choledochal- pancreatic-biliary junction
- **Infantile form** presents at 1-3 yrs of age with triad of obstructive jaundice + acholic stools + hepatomegaly.
- **Adult form** presents at ~2 yrs of age with triad of pain

abdomen + mass + jaundice. 50% of patient present after 10 yr. of age

- ↑ risk of cholangiocarcinoma is seen with type IV.
- Dx : USG is IOC; Cholangiography (PTC or ERCP) is gold standard
- T/t : Cyst excision and 'Roux-en-Y' biliary-enteric anastomosis i.e. hepatico-jejunostomy is the procedure of choice. (Drainage is NOT done).

→ 'Central dot' sign is seen in Caroli's d/s (type V CDC).

→ 'Comet tail' sign is seen in adenomyomatosis of GB or in emphysematous cholecystitis.

EHBA(Extrahepatic Biliary Atresia)

- EHBA is a condition in which there is inflammation with stricture of hepatic or common bile duct. Also k/as extrahepatic ductopenia" and "progressive obliterative cholangiopathy" is a congenital or acquired disease.
- CMV, reo, rota viruses & TH1 & interferon γ are involved in pathogenesis.
- Kasai operation is done. Portoenterostomy is the only available t/t, with better results when performed in the first 2 months of life.
- All untreated children eventually die due to complications resulting from portal hypertension and liver cirrhosis.
- M/c indication of liver transplantation in children.

PLASTIC & RECONSTRUCTIVE SURGERY

Z-Plasty

- Transposition flap used frequently for tissue transfer into a scar/contracture.
- Also used for lengthening/ reposition of scar within lines of minimal tension.

Axial flaps

- Contain cutaneous vessels running in the longitudinal axis of the flap. e.g.
- Examples are:
Midline forehead flap : based on supratrochlear vessels and is commonly used for nasal reconstruction
Deltopectoral flap : based on perforators of internal mammary a. used for head, neck defects (cervico-facial surgery).

Various types of tissue coverage/Grafts

Type of wound	Type of coverage	Reason for choice
Mildly infected (< 10 ⁵) wound including burns	Thin STG or meshed graft	Take of thicker grafts is difficult. Donor site may be reused sooner.
Significantly infected (> 10 ⁵) wound (Osteomyelitis etc.)	Thin STG/ meshed or myo-cutaneous flap	Rich vascular supply can sterilize an infected wound
Small facial defect, cleft lip	FTG	Best aesthetic result
Larger facial defect	Thick STG or flaps	FTG cannot be used b/c of limited donor site
Full thickness eyelid loss	Local flap/ composite graft	Repair require > 1 tissue element
Deep loss of nasal tip	Local flap/ composite flap	Thick tissue required
Nasal reconstruction	Paramedian forehead flap	
Avulsive tissue with exposed tendons and nerves	Flap	Thick tissue required
Exposed cortical bone/cartilage	Skin or m/s flap	Frec graft do not survive on avascular recipient site
Nasal reconstruction	Paramedian/ forehead flap	
Radiation burn wound	Muscle/myo-cutaneous flap	Frec graft do not survive on avascular recipient site

Full Thickness Grafts (FTG)

- FTG includes epidermis + complete dermis
- FTG may be taken from the areas of thin skin (or where skin c/b removed without causing scarring problems) like ear, upper eyelid, or scalp. It may also be taken from skin above collar bones, upper and inner arm, groin area, supraclavicular, antecubital, inguinal, genital area or areola.
- It is usually taken from the area.
- FTG can NOT be taken from elbow.

→ Split-thickness grafts (STG) have a greater chance of surviving but will contract upto 40% on average.

→ Flaps are useful for closing defects too large for primary closure and where skin grafting is inadequate (examples are exposed structures such as brain, blood vessels, bone and joint surfaces, wounds with poor vascularity, full-thickness defects in head and neck).

→ Abey Elzander flap is used for reconstruction of lower lip

Breast reconstruction

- Use of silicone implants/expanders.
- Flaps for coverage
 - Latissimus dorsi flap (M/c pedicle flap)
 - Trans. Rectus abdominis musculocutaneous (TRAM) flap (m/c free flap).

Graft survival

- In the first 48 hr skin grafts survive by the process of plasmatic imbibition.
- After 48 hrs. graft survival depends upon microvascular buds formation (inosculation)
- For successful survival of a graft vascularization is most important.

Graft for various conditions

Condition	Suitable flap/Graft
1. Plastic repair of nose	Paramedian forehead flap
2. Reconstruction of upper eyelid	FTSG (for >50% defect), Tarsal graft, Tenzel flap, OMAF in older patients with large FT defect
2. Reconstruction of lower eyelid defects	Temporoparietal fascial flap (TPF)
2. Reconstruction of cheek	Radial forearm > ALT flap
4. Ear reconstruction	Antia flap (from helix)
5. Reconstruction of upper lip if oral commissure involved	Karapandzic, Eastlander flap
6. Reconstruction of lower lip, angle	Abbe flap from upper lip
7. Cervico-facial surgery	Deltpectoral flap
8. Plastic repair of sternum incision	Pectoralis major
9. Lower limb injuries	ALT (Fascia + skin from anterolateral thigh) flap is least morbid flap

POINTS OF SPECIAL MENTION

- In T/t of SqCC of Anal canal -- Chemoradiation is used and if recurrence -- APR (Abdomino-perineal resection).
- In Ca rectum (lower part) -- APR is used, & if recurrence -- chemoradiation
- In Ca-rectum (upper part) > 2.5 cm. above dentate line -- Low ant resection

(or 1cm above anal verge)

- Small bowel is the most frequently injured organ after penetrating injury (Sabiston)
- Spleen is the intra-abdominal organ most frequently injured in blunt trauma
- Among adenoma of G.I.T. - Tubular adenomas are m/c and Villous : most malignant.
- Raised Gastrin level without associated increase in gastric acid secretion is seen in --- Pernicious anemia.
- Superficial part of parotid overlies - Ramus of mandible + Masseter.
Deep part of parotid overlies --- Space behind medial pterygoid + tonsil.
- M/c site of solitary rectal Ulcer - Ant. Wall Midline.
- **Goodsall's rule** - Fistulae with an external opening in relation to anterior half of anus tends to be of the direct type (have straight tracks) while fistulas in relation to post. half of anus (which are more common) have curving tracks and may be of horse shoe variety.
- **Revised Trauma scores** includes - Glasgow coma Scale + RR + Systolic BP.
- **Mammography** is the most useful technique for early detection of breast cancer and is most sensitive.
- Diagnosis of breast cancer depends ultimately upon examination of tissue / cells removed by biopsy.
- Muscle is strengthened by Resection / Dissection.
Weakened by recession
Rest is given to muscle by tenotomy.
- Best T/t of infected subaponeurotic hematoma --- I & D.
- M/c c/c of jejunostomy feeding --- Diarrhoea
- M/c site of aortic rupture --- Ligamentum arteriosum
- M/c site of fasciotomy --- Calf
- M/c cause of leg ulcer --- Venous ulcers
- M/c cause of gastric outlet obstruction in India --- Gastric cancer
- M/c cause of upper g.i. bleeding --- Peptic ulcer
- M/c cause of lower g.i. bleeding --- Non-specific ulcers
- Acanthosis nigricans is commonly seen in :Ca Gastric > Uterine Ca > Lung Ca (GUL)
- Intrahepatic lesions produce major resistance to flow of portal blood is on hepatic venous side of sinusoids (post-sinusoidal) but in congenital hepatic fibrosis & schistosomiasis major resistance to blood flow is pre-sinusoidal.
- Multiple fistula in ano results from TB (commonest), Crohn's disease, UC, LGV, Bilharziasis.
- Enterovesical fistula (causes according to sabiston) Diverticulitis (>50%) > Colorectal ca.(16-18%) > Crohn's

disease (13-15%) > Bladder Ca. (12%).

- Colovesical fistula (causes): Diverticulitis (>50%) > granulomatous colitis (18%) > Colorectal ca.
- Hardy was the first surgeon to do proximal ureteric implantation.
- 8 yr old girl was found hypertensive. M/c cause is --- Chronic glomerulonephritis
- Grayhack shunt is the shunt for priapism made b/w corpora cavernosa and corpora spongiosa.
- A 50 yr old male presented with Hb 10 gm%. Occult blood is +ve. Next Ix of choice is --- Colonoscopy
- Strassburg classification of cystic duct blow out is an example of type A or Grade I
- Early complication seen in ileostomy --- Diarrhoea
- Morgagnian hernia is most commonly through --- Foramen of Morgagni (Right anterior hemidiaphragm)
- Incision is always given in midline in case of blunt injury abdomen.
- Best way to get bile drainage in donor liver --- Donor bile duct with recipient bile duct (duct to duct anastomosis).
- Any diverticulum, which is congenital has all layers e.g. MD (Meckel's diverticulum). Acquired diverticula does not contain all layers.

M/c Gas in

- M/c gas produced in intestinal obstruction --- N_2
- M/c gas produced in Clostridial infection --- H_2S
- M/c gas used to create pneumoperitoneum (in laparoscopy) --- CO_2

SOME IMP. NEGATIVE POINTS

- Removal of 90% of jejunum and ileum will NOT lead to --- Hypogastrinemia, water intoxication.
- NOT seen in short bowel syndrome --- Hypogastrinemia
- Intestinal biopsy is NOT used for D/g of --- Blind loop syndrome.
- Incidence of Gall stones is NOT increased after --- jejunal resection.
- Peptic ulcer is NOT associated with --- PV syndrome, pernicious anemia
- Spontaneous regression is NOT seen in --- Osteosarcoma
- Acute pancreatitis is NOT caused by --- Hemosiderosis
- NOT included in Ranson's prognostic criteria in pancreatitis --- \uparrow amylase, Hypercalcemia, \uparrow PT.

- Does NOT correlate with severity of acute pancreatitis --- Serum amylase.
- Serum amylase is NOT raised in --- Acute appendicitis
- Medullary carcinoma of thyroid is not a --- Hormone dependent tumour.
- FNAC is NOT useful in --- Follicular carcinoma
- NOT seen in subacute thyroiditis --- \uparrow RAIU
- Swelling which does NOT move on deglutition --- Sublingual dermoid
- Colonic pseudoobstruction is not seen in --- Hyperthyroidism
- B/L parotitis not occurs due to --- SLE
- Acute parotitis not occurs due to --- Candidiasis
- Lumbar sympathectomy is not done for --- Claudication pain (walking pain)
- Burger's disease is not related to --- Atherosclerosis, DM, Old age.
- In Whipple's procedure structure not removed --- Portal vein.
- Linitis plastica is not seen in --- Leiomyosarcoma
- Thoracotomy is not indicated for --- Pulmonary contusion
- In Insulinoma not seen --- weight Loss.
In Pheochromocytoma not seen --- Weight gain during 1st week of IV hyperalimentation not seen --- Weight gain
- Lung abscess are usually not seen in --- Mycoplasma pneumoniae & Bronchopneumonia.
- Thymoma is not a/w --- Hypergammaglobulinemia
- not a C/c of Lymphedema --- Hypoproteinemia
- Chronic lymphedema does not cause --- Marjolin ulcer
- In Radical ND structures not removed are --- Ext. carotid a., facial nerve, phrenic nerve.
- Structures not removed in radical mastectomy --- Supra-clavicular LN
- DIC is not seen in --- Breast Ca.
- Large breast are not seen in --- Scirrhus Ca (shrinkage of breast tissue occurs in it).
- NOT a risk factor for Ca. breast --- Multiparity.
- NOT a extra gonadal GCT site --- Prostate.
- NOT seen in undescended testis --- Hydrocele
- NOT true about Rupture of bulbar urethra --- Floating prostate on PR & # pelvis
- Prostatic plexus not communicates with --- Sup. rectal veins.
- NOT predisposes to Ca. UB --- TB cystitis.
- NOT elevated in a child presenting with jaundice, icterus, clay colored stools, pruritus --- Glutamate

dehydrogenase..

- o NOT true about Erysipelas ---- It is contagious.
- o Complication which usually do not occur after hemithyroidectomy ---- Palsy of external branch of superior laryngeal nerve (ELN)
- o NOT a cause of DVT ----DM
- o In bronchoscopy structure NOT visualised --- Sub carinal lymph nodes.
- o NOT true of xanthogranulomatous pyelonephritis --- A/w TB
- o NOT a restrictive bariatric surgery --- Duodenal switch

CLINICAL VIGNETTES

- A 20 year old male was brought to casualty with 30% burns. Amount of fluid required to resuscitate this patient in first 24 hours is- [DNB MAMC 2008]

A. 2000 mL B. 3000 mL
C. 7000 mL D. 9000 mL

(Ans.: D.7000 mL)

Parkland's formula is used for fluid resuscitation in burn patients.

Total fluid required in 24 hours is = 4 ml/kg/% of burn . Half of this is given in first 8 hours, 1/4th in next 8 hours and remaining 1/4th in next 8 hours

As a reference Indian man weighs 60 kg on average, total fluid requirement for him would be $4 \times 60 \times 30 = 7200$ mL.

- A 35 year old male patient presented with hematemesis and melena for 2 days. Upper GI endoscopy was found to be normal. He had a rebleed in the hospital. What should be the next step?
- A. Urgent Enteroscopy
B. Urgent Angiography.
C. Repeat Upper GI endoscopy at the time of re-bleed.
D. Surgery.
- (Ans.: B. Urgent Angiography)
- A 70 year old patient with BPH underwent TURP under spinal anaesthesia. One hour later, he developed vomiting and altered sensorium. The most probable cause is-

A. Overdose of spinal anaesthetic agent
B. Rupture of bladder
C. Hyperkalemia

D. Water intoxication

(Ans.: D. Water intoxication)

D/d of C/c of TURP

Water intoxication is a common feature of TURP syndrome, a complication noted either intraoperatively or post operatively within 24 hour of TURP if water or any other hypotonic solutions e.g. sorbitol is used for irrigation . It is characterized by altered sensorium, confusion, visual disturbances.

If there is **overdose of spinal anaesthetic agent**, symptoms will appear within 5-10 min.

- A 70 year old male underwent transurethral resection of prostate. On the third post operative day developed abnormal behaviour and became drowsy. The most probable reason is:

A. Meningitis following spinal anaesthesia

B. Cerebral infarction.

C. Hyponatremia.

D. Hypernatremia.

A (Ans.: C. Hyponatremia)

Hypo-osmolality is the basic pathology not the hyponatremia, which is responsible for neurological symptoms after TURP. However hyponatremia occurs secondary to water intoxication (Dilutional hyponatremia)

- A 20 year old male comes with complaints of high fever since 10 days. He has acute pain in whole abdomen. O/E there is guarding and board like rigidity. Most likely cause is- [DNB MAMC 2008]

A. Gastric perforation B. Duodenal perforation
C. Enteric perforation D. Acute appendicitis

(Ans.: C. Enteric/ ileal perforation)

Hx of high grade fever for 10 days goes in favor of typhoid fever (Enteric fever) . Enteric perforation can occur in 2nd or 3rd week of fever.

- A 70 year old male patient presented with history of chest pain and was diagnosed to have coronary artery d/s. During routine evaluation, an ultrasound of the abdomen showed presence of gall stones. There was no past history of biliary colic or jaundice. What is the best t/t advice for such a patient for his GB stones:

A. Open cholecystectomy
B. Laparoscopic cholecystectomy
C. No surgery for gallstones
D. ERCP and removal of stones

(Ans.: C. No surgery for gallstones)

The pt is elderly and asymptomatic--- no need for surgery
If the pt is young then answer would have been ---
laparoscopic cholecystectomy bec risk of GB cancer
increases per year by 0.5-1%

- A 30-year old male is brought to casualty after a road traffic accident with complaints of pain in upper abdomen and left lower chest. At presentation, the patient is hypotensive but becomes hemodynamically stable after initial resuscitation. The abdominal examination reveals mild tenderness in upper abdomen. The abdomen is soft and there is no distension. Chest radiograph reveals fracture of 9th and 10th ribs on the left side. There is no hemothorax or pneumothorax. The patient should undergo. [AIPGMEE' 2008]

A. Immediate laparotomy
B. Further abdominal imaging to rule out intra-abdominal injury
C. Serial observation
D. CT scan of the chest

(Ans.: B. Further abdominal imaging /Abdominal CT to rule out intra-abdominal injury)

- A 27 year old comes presents to emergency room with left sided pain abdomen after a road traffic accident. He was hemodynamically stable and FAST +ve . CECT showed grade II lacerations. What is the most appropriate treatment [AIPGMEE' 2010]

A. Conservative treatment
B. Splenectomy
C. Splenorrhaphy
D. Splenic artery embolization

(Ans.: A. Conservative treatment)

- **FAST ultrasound** (Focus Abdomen Sonogram for Trauma patient) should be done in all trauma patients. It includes a quick assesment of pericardium, pleural space, liver, spleen and Morrison's pouch
- **Conservative t/t is advised** --if there is partial tear, small subcapsular tear, patient is hemodynamically stable
- **Splenectomy is advised** ---For hilar injuries, pulverized splenic parenchyma, grade 2 or + injury in a pt of coagulopathy
- **Splenic artery embolization is indicated** --Grade III laceration, contrast leak in CECT (bleeding patient).

- A 27 year old comes presents to emergency room with left sided pain abdomen after a road traffic accident. He was hemodynamically stable and FAST +ve . CECT showed contrast blush along with grade III lacerations. What is the

most appropriate management [AIPGMEE' 2010]

A. Conservative treatment
B. Splenectomy
C. Splenorrhaphy
D. Splenic artery embolization

(Ans.: D. Splenic artery embolization)

- 1 year After cholecystectomy, a patient presented with 2.5 cm size stone in CBD, Treatment of choice is:

[AIPGMEE – 1999]

A. Choledocholithotomy with T-tube drainage
B. Supraduodenal choledochotomy with exploration
C. Trans duodenal choledochojunostomy with sphincteroplasty
D. Endoscopic sphincterotomy with stone extraction

(Ans: D. Endoscopic sphincterotomy with stone extraction)

- A 6 year old girl presents with recurrent E. coli infection in urine. Ultrasound of abdomen shows hydroureter and Hydronephrosis. Micturating cystourethrogram shows filling defect in urinary bladder. The likely diagnosis is:

[AIPGMEE – 2000]

A. Sacrococcygeal Teratoma
B. VUR, Grade-II
C. Duplication of Ureter
D. Ureterocele

(Ans: D. Ureterocele)

- A 9 year boy presented with abdominal pain and recurrent UTI, IVP reveals duplication of left ureter. The most likely site of ectopic opening would be: [AIPGMEE – 1999]

A. Prostatic urethra
B. Ejaculatory duct
C. Seminal vesicle
D. Vas-deference

(Ans: A. Prostatic urethra)

- A male presents with azoospermia. On examination size of testis is normal, FSH and testosterone normal. Probable cause is:

[AIIMS Nov'09]

A. Undescended testis
B. Klinefelter's syndrome
C. Kallman syndrome
D. Vas obstruction

(Ans.D. Vas obstruction)

Azoospermia in a patient with normal testicular biopsy report (size of testis is normal, functions of testes are normal

hence FSH and testosterone levels are normal) is very much suggestive of obstruction of vas deferans. It is a surgically correctable condition.

Klinefelter's syndrome is c/by --- Azoospermia + ↓ FSH, ↓ testosterone + small testes

Kallman's syndrome is c/by --- Anosmia + ↓ GnRH, ↓ FSH, ↓ testosterone + small and soft testes

Cryptorchidism or undescended testes are c/by --- Oligospermia + ↓ FSH, ↓ testosterone + small testes

- 15 yr old child presents with right sided hydronephrosis and left flank pain. DTPA shows 19% renal enhancement, 10 mm thickening of renal parenchyma. Treatment is :
[AIPGMEE'10]

- A. Pyeloplasty
 - B. Nephrectomy
 - C. Endopyeloplasty
 - D. External drainage
- (Ans. A. Pyeloplasty)

Renal parenchymal thickening of 10 mm, 19% renal enhancement are suggestive of CRF. Obstruction should be relieved immediately by pyeloplasty.

- A patient presents with 10 mm calculus in the right lower ureter a/w proximal hydroureteronephrosis . Best t/t is
[CGPPG'2009]

- A. ECSWL
 - B. Open ureteroscopic retrieval
 - C. Antegrade percutaneous access
 - D. Ureteroscopic retrieval
- (Ans: D. Ureteroscopic retrieval)

- Ureteroscopic retrieval is preferred for distal small stones.
- Open removal is done if stone is large and URS is not available
- ECSWL is preferred for most oxalate and phosphate stones lying in renal pelvis. ECSWL is not indicated for cystine stones because they are hard and difficult to break. One imp. C/c is impaction in distal ureter which may lead to ureteric colic and require URS.

- 25 yr female presents with b/L large impacted stones in the proximal ureter with urea 220 and serum creatinine 14. Next line of m/m is: --
[[CGP[AIPGMEE'10]009]
- A. B/L ureterolithotomy
- B. Ureteroscopic retrieval
- C. B/L DJ stenting

D. Hemodialysis

(Ans: D. Hemodialysis)

Patient is in CRF and urea 220 and serum creatinine 14 values are very high requiring urgent hemodialysis.

- In 45 years old male patient presented with injury to left renal artery, aorta, and celiac plexus . Which of the following procedure you will do? [AIIMS May'10]
 - A. Right medial Visceral rotations
 - B. Left medial Visceral rotations
 - C. Cranial rotation of gut
 - D. Caudal rotation of gut
- (Ans.B. Left medial visceral rotations)

Some maneuvers are recommended while doing surgeries on large vessels. Left medial visceral rotation (Mattox maneuver) provides excellent exposure to aorta, celiac axis, superior mesenteric artery, left renal artery and iliac arteries.

Right medial visceral rotation (Catell maneuver) provides exposure to vena cava, right renal vessels and iliac veins.

- A Patient brought to the hospital with the history of RTA with pelvic fracture 8 hours ago. A few drops of blood was noted in the external urethral meatus. He had not passed urine and his bladder is palpable per abdomen. What is the probable diagnosis. [AIIMS May'10]
 - A. Anuria due to hypovolemia
 - B. Urethral injury with extravasation of urine in retroperitoneum
 - C. Urethral injury
 - D. Rupture bladder
- (Ans.C.Urethral injury)

Bulbar urethra is the m/c site of urethral injury and is c/ by retention of urine + perineal hematoma + blood from EUM. Common in RTA, astride injuries, cycling injuries. Extravasation of urine in retroperitoneum is seen in --- extraperitoneal rupture of bladder or membranous urethra injury

- A patient underwent lap cholecystectomy for cholelithiasis. Post-op pathological examination revealed adenomatous carcinoma invading the muscular layer and not spreading beyond. What should be the next step in management?
[AIIMS Nov'09]

- A. Regular follow up with USG
- B. Chemotherapy with radiotherapy
- C. Wedge resection of liver
- D. Perihilar lymphadenectomy

(Ans. A. Regular follow up with USG)

Carcinoma GB invading muscularis (T1) are usually discovered incidently. Simple cholecystectomy is adequate t/t and results in 100% 5 yr survival. Only regular follow up USG is sufficient.

Wedge resection of liver segments IV B and V is indicated for T₂ tumours (upto serosa).

Tumour excision + Extended right hepatectomy must be done for T₃/T₄ tumours (beyond serosa)

- A patient, on 2nd post op day of THR, develops pain in chest, hypotension and respiratory distress. ECHO shows right ventricular motion abnormalities with TR. The most probable cause: [AIPGMEE'10]

- A. Myocarditis
- B. Acute MI
- C. Constrictive pericarditis
- D. Pulmonary embolism

(Ans.: D. Pulmonary embolism)

Pulmonary embolism is suspected if a patient, develops triad of hypotension + chest pain + respiratory distress. THR is an important risk factor for PE. Rt ventricular dysfunction may develop as indicated by right ventricular motion abnormalities with TR on ECHO.

- A patient presents with stab injury in left hypochondrium. CT scan shows 2cm laceration in liver. Patient was hemodynamically stable until undergoing laparoscopy. As soon as pneumoperitoneum was created pCO₂ increases, PaO₂ falls and patient collapses. The most probable cause: [AIPGMEE'10]

- A. Pressure on IVC
- B. Left diaphragm rent
- C. Transverse colon injury
- D. Air embolism through splenic artery

(Ans.: B. Left diaphragm rent)

Left diaphragm rent is suspected if a patient, during laparoscopic surgery develops lung collapse, hypoxia, and shock. It is d/to CO₂ has entered the rent in diaphragm causing above picture.

Transverse colon injury will lead to peritonitis and septicemia after a few days.

- A 60 yr male taking aspirin since 2 years for coronary artery disease developed black colored stools since two days. Abdominal examination was normal. What is the most probable diagnosis? [AIIMS Nov'09]

- A. Duodenal ulcer
 - B. TB
 - C. Ca colon
 - D. Esophageal varices
- (Ans. A. Duodenal ulcer)

Black colored stools in a pt taking aspirin suggest old blood in stools d/to upper GI bleeding. M/c complication of PUD is hemorrhage. Risk of bleeding is further increased by NSAIDs especially aspirin in Duodenal ulcer patient. Ca colon and TB can present with hematochezia (fresh blood in stools).

Esophageal varices generally present with hematemesis (vomiting of massive blood).

- A person is brought to the trauma centre with blunt abdominal trauma. He is hemodynamically stable. What is the most appropriate step for diagnosis? [AIIMS Nov'09]

- A. Plain X-Ray abdomen
 - B. FAST
 - C. DPL
 - D. Barium enema
- (Ans. B. FAST)

- FAST ultrasound should be done in all blunt trauma patients for quick assesment of pericardium, pleural space, liver, spleen, and Morrison's pouch.
- Blunt trauma patient with hemodynamic instability --- DPL is advocated
- CT is indicated for hemodynamically stable patients if physical examination is unreliable.
- Stab wound patients without peritoneal signs evisceration, or hypotension benefit from DPL.
- Gunshot wound victims should generally undergo --- Exploratory laparotomy
- Hypotensive patients with isolated penetrating abdominal trauma + shock/hypotension or peritoneal signs should undergo operative procedure.

- 10 days old newborn was brought with c/o distension of abdomen, billious vomiting, suspected volvulus with perforation. Next line of investigation is --- [AIPGMEE'10]

- A. Plain X-Ray abdomen
- B. Barium enema
- C. Barium meal

D. Upper GI endoscopy

(Ans. Plain X-Ray abdomen)

If obstruction is suspected d/to malrotation with volvulus, it is a surgical emergency. Upper GI contrast series should be done but in presence of perforation contrast series are contraindicated and it is better to do plain X ray abdomen and then plan laparotomy.

- Young female presents with recurrent fasting hypoglycemia and ↑ insulin . USG shows 8 mm lesion in the head of pancreas, fasting insulin and CT scan clinches the diagnosis. Appropriate t/t of this condition is [AIPGMEE'10]

- A. Whipples procedure
- B. Enucleation alone
- C. Enucleation + antrectomy
- D. Trial of streptozocin before undergoing surgery

(Ans. B. Enucleation alone)

Recurrent fasting hypoglycemia and ↑ insulin supported by CT are s/o insulinoma. Majority of insulinomas are benign and solitary and cured by simple enucleation.

- A patient with ITP has a platelet counts of 50,000. He is being planned for splenectomy. Best time for platelet transfusion in this patient. [AIPGMEE'10]

- A. 2 hours before surgery
- B. At the time of skin incision
- C. After ligating splenic artery
- D. Immediately after splenectomy

(Ans. C. After ligating splenic artery)

Platelet transfusions are generally withheld until the splenic vessels have been controlled at operation.

- A child presents with recurrent abdominal pain and billious vomiting. Barium follow through was done to establish a diagnosis. Surgical procedure was done and Ladd's bands divided, appendicectomy and mesenteric widening done. Diagnosis is: [AIIMS Nov'10]

- A. Caecal volvulus
- B. Malrotation
- C. Acute appendicitis
- D. Duodenal web

(Ans. B. Malrotation)

Plain X-ray is non specific , however Ba follow through will clinch the diagnosis in malrotation. Further the typical surgical procedure gives clue to malrotation. Midgut volvulus and malrotation are fire brigade emergency in children. surgeon should be involved as early as possible.

- A surgeon who is not experienced in laparoscopic CBD exploration finds a stone in CBD while performing a lap cholecystectomy. What should he do next? [A I I M S Nov'11]

- A. Laparoscopic exploration of CBD
- B. Laparoscopic CBD stone extraction
- C. Convert to open cholecystectomy and CBD stone extraction
- D. Open cholecystectomy and choledochoduodenostomy.

(Ans.: C. Convert to open cholecystectomy and CBD stone extraction)

NOTES

PHYSIOLOGY

Menstrual Cycle

- Normal menstrual cycle has a periodicity of 28 days. Timing of ovulation is more consistent with 2nd half of cycle. Ovulation occurs 14 days prior to next menstrual cycle.

There are 4 phases of this cycle

1. Menstrual/ bleeding phase 1-5 days
2. Proliferative (follicular, estrogenic) phase (6-13 days)
3. Ovulatory phase (14-16 days)
4. Secretory (progestational/ leuteal) phase (16-28 days)

1. Menstrual/ bleeding phase (day 1-5)

Beginning of the bleeding is considered day 1 of m.c. 2/3rd of thickness is shed off and stratum basale remains intact. Post menstrual endometrial thickness (ET) is 1 mm.

2. Proliferative (follicular, estrogenic) phase (day 6-13)

Ovarian follicles grow under influence of estrogens. Epithelial regeneration occurs.

3. Ovulatory phase/ Ovulation (day 14)

LH surge is central to the ovulation process. LH surge precedes ovulation by 24-36 hours. Mid cycle peak of LH induces ovulation. LH surge is triggered by an estradiol peak in the late proliferative phase of cycle. 4 P's responsible for ovulation are: proteolytic enzymes, progesterone induced FSH rise, plasminogen activators, prostaglandins. A luteal phase endometrial biopsy has been used to confirm ovulation.

4. Secretory (progestational/ luteal) phase (day 15-28)

It lasts for 13 days (day 15- day 28). In this phase corpus luteum (CL) is formed by ovary after rupture of mature graffian follicles. CL is regulated by progesterone produced by it. Uterine glands become tortuous, saccular. Spiral arteries become coiled. Endometrium is thickest (ET=5-7 mm).

LH surge $\xrightarrow{24-36\text{ h}}$ Ovulation $\xrightarrow{12-24\text{ hrs}}$ Fertilisation

→ Recruitment of follicles is done by FSH

→ Rupture of follicles is done by LH

→ FSH causes growth/ development of follicles during 1st 14 days (first half of cycle), which leads to gradual ↑ in estradiol production from granulosa cells

→ Ovulation depends upon LH & FSH both.

- Withdrawal of progesterone after estrogen priming results in menstrual bleeding:

→ If failure of withdrawal bleeding occurs after estrogen priming → indicates receptor defect or hypothalamic pituitary axis defect

→ A pt of primary amenorrhea showing no withdrawal bleeding after estrogen/progesterone t/t → Indicates endometrial cause (Refractory endometrium)

→ A patient of secondary amenorrhea shows bleeding after progesterone withdrawal → it indicates endometrium is oestrogen primed but there is anovulation (?Luteal phase defect)

Corpus Luteum (CL)

- LH is responsible for initial formation of CL. Maintenance of CL depends on hCG produced during pregnancy.
- In absence of pregnancy CL begins to degenerate on 24th day of cycle & eventually replaced by corpus albicans.
- In pregnancy: Max^m growth of CL of pregnancy is at 8 weeks of gestation and starts degenerating at 6 months
- CL secretes --- progesterone, estrogen, inhibin, relaxin, androstenedione (by theca cells)

Progesterone

- Corpus Luteum (granulosa luteal cells) is the major source of progesterone (in form of 17-αHP) during 1st trimester. After 12 wks placental trophoblast cells are major source.
- Major substrate for progesterone synthesis is maternal cholesterol. The luteal phase of the menstrual cycle is characterized by high circulating progesterone concentrations. Cutoff values of progesterone that ovulation has occurred are 4 ng/mL to 10 ng/mL.
- Plasma levels rise during pregnancy till term, fall rapidly after delivery, becomes undetectable 24 hrs postdelivery.
12th wk → 28th wk → Term
25 80 300 ng/ml

- P~ maintains normal pregnancy/ keeps the uterus in quiescent stage by relaxing the myometrium.
- It has some **natriuretic** action d/to \uparrow aldosterone. (In pregnancy salt intake should be proper)
- *Fetal synthesis contribute little to maternal level, therefore P~ level will remain high even after fetal demise.*

→ \downarrow progesterone levels are seen in --- Ectopic pregnancy, abortion

→ \uparrow progesterone levels are seen in --- H. mole, Rh-immunization

→ Arias Stella reaction and decidual reactions occur under the influence of progesterone

ESTROGEN

- Secreted primarily by **granulosa cells** of ovarian follicle and also by CL. Synthesized either from androgens or by aromatization of androstenedione.
- Estrogen synthesis from endometrial stromal cells is upregulated by **aromatase**.
- Produced in late pregnancy by placental **syncytiotrophoblasts**.

- *Conditions a/w \downarrow estrogen in blood*
Menopause, Lactation, Surgical castration, during endometriosis T/t.

- *Conditions a/w \uparrow estrogen in blood*
OCP therapy

- Naturally occurring estrogens are : 17 β - estradiol, estriol and estrone.

Estradiol -- Most potent and major estrogen of blood in normal individuals.

Estriol -- Major estrogen in pregnancy and marker of fetoplacental unit.

-- Maximum excretion in urine

Estrones -- Major estrogen in post menopausal women.

Estriol

- Estriol is the most important form of estrogen. It is the marker of adequacy of materno -feto- placental unit (indicates fetal well-being). Produced mainly by fetal adrenals. Estriol is first detectable at 9 weeks (0.05ng/mL) which \uparrow es till term. Salivary estriol is predictor of preterm labour
- Estriol \uparrow es placental blood flow. In pregnancy there is 1000 fold \uparrow (max^m) in urinary estriol

Causes \uparrow in serum binding proteins (which leads to falsely elevated thyroxine & cortisol level).

→ \downarrow Estriol levels are a/w --- Fetal deaths, h.mole, fetal anomalies (adrenal atrophy/anencephaly/Down's), placental sulfatase/aromatase deficiency

hCG

- Glycoprotein hormone chemically & functionally similar to pituitary LH or TSH.
- A single gene located on chromosome 6 encodes the α -subunit for hCG, LH, FSH, and TSH. There are 7 separate genes on chromosome 19 encode for β -hCG and β -LH
- Its β -subunit is specific (β -hCG). It c/b measured by ELISA. Urine test is usually based on chromatographic immunoassay.
- Half life is 24 hours.
- In early pregnancy (before 5 weeks), hCG is synthesized/ expressed in both syncytiotrophoblasts and trophoblasts cells of blastocyst but later (eventually) by **syncytiotrophoblasts** of placenta.
- hCG enters maternal blood at the time of blastocyst implantation.

hCG levels :

In maternal plasma start rising 8 days post-ovulation (post conception) & concentration doubles every 2 days. It reaches peak (100 IU/ mL) at 8-10 weeks. Secondary peak occurs at 32 wk.

In fetal plasma have similar pattern but contribute only 3% of maternal plasma levels of hCG.

In amniotic fluid have similar pattern in early pregnancy but levels decline as the pregnancy approaches near term (hCG levels are only 20% of that of maternal plasma levels)

In maternal urine correlates maternal plasma levels. Peak levels are seen at around 10 weeks.

- Disappears from urine 2 days & from blood 2 wks after delivery.

- hCG stimulates progesterone production by CL of pregnancy (*LH like action*).
- hCG stimulates Leydig cells in male fetus and thus development of male genitalia.
- Gestation sac is formed 100% (completely) at β -hCG level of 2400.
- Minimum β -hCG concentration that blood serum test can detect is 5 mIU/mL & in urine it is detectable at 25 - 50 mIU/ml, so the blood serum is more sensitive.

- During normal pregnancy there is exponential rise in serum hCG levels and there is double peak
- Relatively high (\uparrow) hCG levels are seen in --- Fetus with Down syndrome (21 trisomy)
- Abnormally high ($\uparrow\uparrow$) hCG levels are seen in
 - Multifetal pregnancy (e.g. twin gestation), erythroblastosis fetalis a/w fetal hemolytic anemias, and molar pregnancy/ gestational trophoblastic d/s. (eg. > 1,00,000 mIU/ml at 15 wk gestation may be seen in choriocarcinoma)
- \downarrow hCG levels (plateauing) are seen in --- Ectopic pregnancy, abortion/ early pregnancy wastage

Arias stella reaction

- Non specific reaction d/to steroidal hormones (reaction to estrogen and gonadotropins)
- Seen in ectopic pregnancy, molar pregnancy, choriocarcinoma, endometriosis

PREGNANCY CHANGES

Anatomical

- Placenta weighs 500 gm at term.
- Uterus weight \uparrow es from 50 gm to \rightarrow 1000 gm at term.

Physiological

- Hypervolemia. Blood volume is + 40-50%, reaches max^m at 30-32 weeks. RBCs volume (hct) is +20-30% which leads to hemodilution resulting in *physiological anemia of pregnancy*.
- Amniotic fluid volume reaches max^m at 36-38 wk \sim 1 L.
- Vital capacity, respiratory rate and clotting time ---remains unchanged.
- SBP = N, $\downarrow\downarrow$ DBP so \uparrow in PP \uparrow in HR
- \uparrow Cardiac output by 40% (max^m at 30-34 week & continue at this level till term).
- Systolic ejection murmur are seen in >90% pregnant women.
- Blood: \uparrow in ESR, TLC
- \uparrow in total plasma proteins. \uparrow Globulin but \downarrow in albumin.
- \uparrow in TIBC, S. transferrin \uparrow while \downarrow in serum Fe, ferritin [Mnemonic: \uparrow in 4't and fall in 2F]

Hormonal

- Moderate hyperplasia of thyroid -- \uparrow T₄, \uparrow TBG, \uparrow BMR (but free T₃ & T₄ are normal)
- Circulating cortisol \uparrow but most of it is bound to transcortin (free cortisol levels are not changed)

Thyroxine & cortisol \uparrow es because of \uparrow in their binding proteins (TBG & Transcortin)

- Maternal pituitary \uparrow es in weight by 30-50% but is not necessary for maintenance of pregnancy.
- Plasma PTH \downarrow in 1st trimester then \uparrow in rest of gestation (estrogen blocks the effect of PTH on bone resorption)
- Total serum calcium \downarrow es (up to 34-36 wk) but ionized Ca⁺⁺ is constant. Calcitonin increased by 20%
- PRL \uparrow es constantly throughout gestation & is maximum at term (10 times of normal)
- Insulin \uparrow (hyperinsulinemia), resistance \uparrow es.
- Aldosterone \uparrow

→ Hormones which do not cross placenta --- ACTH, PTH etc.

- Peripartum cardiomyopathy is dilated (DCM) type, develops in last months of pregnancy or within 6 month of delivery.
- Post partum psychosis develops within 6 months of delivery (Postpartum blues)

Renal changes in pregnancy

- Protein, amino acids and glucose excretion in urine is increased in 3rd trimester. Glycosuria (+nce of glucose in urine) is normally found in 50% pregnant women.
- \uparrow in GFR and so \downarrow in urea, creatinine, BUN
- Unequivocal evidence of heart disease in pregnancy is diastolic murmur and thrill.
- Risk of CCF is maximum in --- at the time of labour
- Fetal growth is maximally affected by --- insulin

Lactation

- Estrogen is lactational suppressant. It inhibits prolactin.
- In pregnancy lactation is suppressed by estrogen and progesterone which block the effect of prolactin.

Changes in lactating women

- After delivery estrogen and progesterone levels are $\downarrow\downarrow$ (low), thus prolactin becomes effective, lactation promoted
- Atrophic vaginitis d/to estrogen withdrawal because normal protective thickness of vaginal epithelium depends upon estrogenic stimulation.
- Estrogen decreases, progesterone levels are maintained and prolactin levels are increased

Criteria for using lactational amenorrhoea method (LAM) for contraception:-

1. EBF (Exclusive breast feeding)
2. No menses since giving birth
3. <6 month post partum

Lactational amenorrhea period is

6 weeks : in mothers who do not breastfeed their babies

6 months: in mothers who do breastfeed their babies regularly

Hormones responsible for changes in breast/ lactation ----

- **Lobulo alveolar proliferation** --- GOPPA [GH, Oestrogen, PRL, Progesterone, Adrenal steroids]
- **Ductal branching & proliferation** --- GOA [GH, Oestrogen, Adrenal steroids]
- **Hormone promoting milk secretion** --- Prolactin
- **Hormone promoting milk ejection or release**--- Oxytocin
- **Hormone maintaining let down reflex** --- Oxytocin (Let down reflex is initiated by sucking at breast by infant)

Drugs affecting Lactation

Induction/ drugs which ↑ PRL Secretion	Suppression
• Anti-psychotic drugs (eg CPZ, Haloperidol)	• Bromocriptine
• Anti-anxiety (Diazepam)	• Levodopa, Other DA agonist
• Anti-hypertensive (Reserpine, methyl dopa)	• Estrogen, DES
• TRH, Testosterone	• Pyridoxine
• Barbiturates	• Apomorphine
• Antidepressants	• MAO inhibitor
	• Cabergoline
	• Thiazides.

- By increasing tubal motility
- Impairment of sperm ascent

Copper containing IUDs

- Prevent implantation by enzymatic interference.
- **Gynefix** consist of 6 Cu cylinders on a nylon thread, a/w excessive early expulsions.
- **Cu-T 380 A (Paragard)** has very long life of 10 years

Hormonal IUDs

Levonorgestrel (LNG) containing IUDs

- Act by suppression of endometrium, rendering the cervical mucous thick. They also cause anovulation & lack of luteal phase.
- **Mirena** contains 52 mg of LNG & releases @ 20 µg/d and is effective upto 5 yrs.
- **Skyla** contains 13.5 mg of LNG

Progesterone containing IUDs

- **Progestasert** releases 65 µg of progesterone which forms a thick mucous plug at cervical os & prevents penetration by sperms. Incidence of menorrhagia & dysmenorrhoea is less.

Effective life of various IUCDs

Cu T 380 A (10yr) > Mirena 5 yrs > MLCu -375 (5 yr) > Cu T 200 (4 yr) > Multiload 250 (3 yr) > Progestasert (1 yr)

Other uses of IUCDs:

- Asherman's syndrome
 - Following excision of uterine septum.
 - Hormonal IUCDs in menorrhagia and dysmenorrhoea.
- C/ind for the use of IUCD: Suspected pregnancy.

→ *Mirena can be used for non-contraceptive therapeutic indications like --- Menorrhagia, endometrial hyperplasia, fibroids, premenstrual syndrome, endometriosis etc.*

CONTRACEPTION

INTRA UTERINE DEVICES (IUDs)

- IUDs are preferred for- multipara, monogamous/ low STD risk patients.
- Probably they act by
 - Biochemical & histological changes in uterine endometrium
 - (Increased leucocyte infiltration in the endometrium i.e. aseptic endometritis)

OCPs (ORAL CONTRA CEPTIVE PILLS)

Combined Pills

- Started on day 5.
- **Mala-D** is a government owned brand of oral contraceptive pill. It is provided at a subsidized price under the Contraceptive Social Marketing Program HLFPT. It contains levonorgestrel-0.15 mg and ethinylloestradiol-0.03mg. Pack also contains 7 tabs of ferrous fumarate 60mg equivalent to ferrous iron 19.5mg.
- **Mala-N** : Contains 30µg of ethinyl estradiol.

Ad/E Related to

Progesterone	Estrogen	Both E+P
<ul style="list-style-type: none"> • Hypertension • ↓HDL (atherogenic) • ↑Blood glucose and plasma insulin. • Breast engorgement • Weight gain • Metabolic effects • Acne • Hypomenorrhea • ↓Libido • Abnormal GTT 	<ul style="list-style-type: none"> • Venous thrombo-embolism • Gall stones • Hypertension? • Menorrhagia • Breast pain / tenderness • Lactation suppression • Chloasma • ↑ Sensitivity of insulin 	<ul style="list-style-type: none"> • Arterial Thromboembolism • ↑BP

→ Combined oral pills ↓ glucose tolerance and cause intensification of pre-existing diabetes. ↑ insulin secretion and create resistance (P)

→ Hepatocellular adenoma and hypertension are most strongly a/w OCP use.

→ Contraceptive failure may be seen with the concurrent use of anti-epileptic drugs. So the use of OCPs is not advised in a women with h/o seizures.

Contraindications of OCPs

Absolute c/ind of OCPs	Relative c/Ind
<ul style="list-style-type: none"> • H/o thromboembolism • Cerebrovascular or coronary HD • Ca-breast / estrogen dependent neoplasia • Undiagnosed abnormal VB (DUB) • Known / suspected pregnancy • Liver d/s 	<ul style="list-style-type: none"> • HTN, DM, Obesity, Hyperlipidemia • Elective surgery • Migraine headache • Uterine fibroid • Sickle cell anemia • Nursing mother (1st 6 mth)

Benefits of OCP's

1. ↓ the risk of Ca-ovary and Ca-endometrium.
2. ↓ benign breast disease or fibroadenoma.
3. ↓ **PID**
4. ↓ Dysmenorrhea, regulates menstrual cycle.
5. ↓ Risk of ectopic pregnancy
6. ↓ risk of functional ovarian cyst.
7. ↓ Anemia by reducing blood loss
8. Rheumatoid arthritis
9. Hirsutism
10. Osteopenia, and osteoporosis

Detrimental effects of OCP's

1. ↑ Risk of Cx cancer, breast cancer (malignant d/s of breast)
2. ↑ Incidence of hepatic adenoma & pituitary adenomas are also reported.
3. ↑ Risk of thromboembolism d/to estrogen.
4. ↑ Risk of chlamydial infection and monilial (candida) vaginitis.

Triphasic combined oral pills (COPs)

Contain EE2 + LNG. Dose is ↑ed during last phase. Carbohydrate and lipid profiles are unaffected and they are safe in **diabetics**. No longer used for contraception

	1-6	7-11	12-21	22-28 days
EE2	30µg	40	30	0
LNG	50 mg	75	125µg	0

• **Femilon** : Contains 0.02 mg EE + 0.15 mg of desogestrel (IIIrd generation progesterone)

• **Novelon** : Contains 0.03 mg EE + 0.15 mg of desogestrel
These are oral pills with improved safety & tolerance profile (low incidence of thromboembolic episodes)

• **Today**: Poly-urathane cotraceptive containing 1gm of Nonoxynol - 9 (spermicidal) effective upto 24 hrs.

• **Implanon**: Non-biodegradable, single rod subdermal implant. Contains 68 mg of etonogestrel (3-keto-desogestrel)

• **Capronor** : Biodegradable, capsule containing LNG

• **Drosperinone**: Structurally similar to spiranolactone but no side effects like wt gain, bloating, and HTN. Low androgenic progestin, so c/b used in conditions of acne, PCOS, and hirsutism. Also used with HRT in menopause to prevent hot flashes and other menopausal symptoms

• **Yasmin** is a newer OCP (EE+ Drosperinone) with lack of androgenic and mineralocorticoid activity. So, there is no water retention or hirsutism.

Once -a- month pill (long acting pill)

Contains long acting estrone (quinestrol) + short acting progesterone.

Mini pill or micropill

Contains progesterone (A type of POP/ progesterone only pill). Recommended in breastfeeding women. Should be avoided in abnormal/ irregular menstrual cycles.

• **Norplant** are LNG containing non-biodegradable

subdermal implants. Obsolete now-a-days

- Silastic Vaginal Ring (SVR) contains LNG releasing 20 mg daily

- *Gossypol is a male pill.*
- *Low dose oral pills contain desogestrels.*
- *Ectopic pregnancies are higher among IUCD & POP users.*
- *M/c cause of PID in IUCD users is Actinomyces Israeli.*
- *M/c infection a/w early abortions - Mycoplasma.*
- *OCPs protect against ectopic, however POP and Post coital estrogen pill increase incidence of ectopic by decreasing tubal motility.*

DEPOT PROGESTINS

- Given by i/m route.
- *DMPA*: 150 mg one i/m injection every 3 months. Initial injections should be given in during first 5 days of menstrual cycle. Useful in post partum period
- *NET-EN*: 200 mg one i/m injection every 2 months.
- *S/E*: Irregular bleeding, weight gain.
- Fertility is regained 5.5 months (3-6 mo range) after stopping DMPA.

Mucous method/Billing method

- Also k/as ovulation method.
- Safe period is from menses until mucous is detected, thereafter the couple must abstain until the 4th day after the peak day

Spermicidal agents

Kill sperms before they enter cervix by altering membrane permeability. These are Nonoxynol-9, octoxynol, menofegol.

CONDOMS (Nirodh)

- A barrier device commonly used during sexual intercourse.
- Failure is mainly d/to improper use > slippage.
- Failure rate 2-3 per 100 women with proper use.

Vaginal Sponge

- Sponge failure rates for women who have never delivered vaginally (nullipara) range from 9% to 16% and 32% in multipara.
- N-9 is released over 24 hr. remains effective 24 hrs after

last coitus.

Calender method (Rhythm method)

- Based on the knowledge of fertile period.
- Fertile period is determined by subtracting 18 days from the shortest cycle and 10 days from the longest cycle, which gives the 1st and last day of fertile period respectively.

Emergency contraception / post coital contraception ("Morning after" pills)

- Morning after pill was old term.
- Emergency contraceptives prevent pregnancy by interfering with post ovulatory events and are therefore k/as **interceptives**
- Oral pills are recommended within 72 hr of an unprotected intercourse. Following methods are used----
- 1. **POP** (containing *levonorgestrel 1.5 mg*) are preparation of choice for postcoital contraception. LNG is the most accepted method for emergency contraception. Dose is 0.75mg given in 2 doses, 12 hours apart within 72 hours or single dose of 1.5 mg.
- 2. Combined pills in double dose are also effective
- 3. Estrogen in high dose
- 4. **Danazol**: A/w androgenic S/E and is costly
- Non-hormonal agents
- 1. **Mifepristone** (RU-486) is effective upto 49 days of LMP
(IUD insertion is a simple method but not recommended for emergency contraception now a days)

Tubal Ligation

- M/c site of fallopian tube ligation for female sterilization is --- Proximal isthmus
- Best recanalisation rate are seen in ---Isthmo-isthmic anastomosis as it gives best results in re-canalization procedures after reconstructive microtubular surgery (tubal ligation reversal)
- Failure rate (Pregnancy rate) of Pomeroy technique is → 0.1%.
- Postpartum Pomeroy (or Modified Pomeroy) Procedure. is the m/c tubal ligation performed in the postpartum period
- Least failure rates are seen with → Bipolar cautery.

Tubal Ligation Reversal

- Tubal ligation reversal is done to achieve pregnancy after a break.
- Success rate or Pregnancy rate after Removal of Falope ring → 50-70%
Reversal of modified Pomeroy → Upto 70%

- Oral contraceptive pill of choice for a lactating women
--- Minipill (POP)
 - Contraceptive method of choice for a newly married couple
--- Combined Oral pills
 - Contraceptive method of choice for a newly married couple of whom female is suffering from RHD, there are ch/nd to use oral pills (like hyperlipidemia, coagulopathy, gall stones) --- Barrier methods.
- Low dose pills can be used in these conditions.
- Contraceptive method of choice for post coital contraception
--- POP (containing 1.50 mg of levonorgestrel).
 - Contraceptive method of choice for Villager female- IUD
 - If both husband and wife are HIV +ve it is advised for them to use condom.

DIAGNOSTIC OBS.

ALPHA FETO PROTEIN (↑ AFP)

In maternal serum (MS-AFP)	In Amniotic fluid (AF-AFP)
Gastroschisis in 98% cases	○ Open NTD
Anencephaly in 90%	○ Ventral wall defect (Gastroschisis / omphalocele)
Open NTD in 75%	○ LBW, Encephalocele
Omphalocele in 70%	○ Erroneous date
(GAOO)	○ Upper GI obstruction (esophageal/ duodenal atresia)
	○ Fetal demise
	○ Cystic hygroma
	○ Renal anomaly (multicystic/dysplastic kidney)
	○ Oligohydramnios
	○ Placental chorio-angioma and infarct

- MS-AFP is NOT elevated in meningocele as it is a closed NTD.
- For early detection of NTDs--- Acetylcholine-esterase is most specific.

Low level of AF-AFP are seen in

- Trisomy 21, 18, 13
- H. mole
- Some cases of fetal demise
- Misdated/ overestimated pregnancy

Synthesis of AFP

- AFP is a glycoprotein synthesized by fetal yolk sac in early weeks of gestation and by the fetal GIT and liver in later part of gestation.
- Concentration of AFP ↑es steadily till 13 weeks (Peak concentration is 3 ng/mL) after which level declines. AFP rapidly clears from circulation soon after birth b/of short half life of 3.5 days
- Peak AFP level in

Maternal serum	30 ng/ml	30-32 nd wk
Amniotic fluid	20,000	early 2nd wk
Fetal plasma / serum	3,00,000	14-15 wk

Double marker assay

- It includes AFP, β-hCG.
- Used for Down's Syndrome detection in patient with advanced maternal age (>35 yrs.)

Triple test

- Also called triple screen, the Kettering test or the Bart's test. It improves the sensitivity and specificity of Down's syndrome detection.
- The test is for screening, not for diagnosis.
- Usually done b/w 15-18 weeks (16 weeks optimum).
- 3 parameters are used AFP, β-hCG, UE3.

	β-hCG	MS-AFP	Unconjugated Estriol (UE3)
Edward syndrome	↓	↓	↓
Down's syndrome	↑	↓	↓
Turner's syndrome	↑	↑	↓

Quadruple test (Quad marker assay)

- Also called tetra screen, quad test, or quad screen.
- Includes maternal serum dimeric inhibin A (DIA) in addition. In Down's syndrome DIA is ↑ ed.

	β-hCG	MS-AFP	UE3	DIA
Edward syndrome	↓	↓	↓	↓
Down's syndrome	↑	↓	↓	↑

- For early detection of Down syndrome---β-hCG is most specific and MS-AFP is the most sensitive marker. PAPP-A, β-hCG & urea resistant neutrophil alkaline phosphatase activity is also used.
- For early detection of NTDs--- Acetylcholine-esterase is most specific.

PRENATAL DIAGNOSIS OF D/S

- Advised for fetuses at ↑ risk for genetic disorders. Parents should be offered genetic counselling:
 - Fetal aneuploidy (Maternal age 35+ is the m/c risk factor for fetal aneuploidy)
 - Familial genetic diseases : There are some **AR** diseases found with ↑ed frequency in certain ethnic groups. E.g Hemoglobinopathies, Thalassemia, IEM (Inborn error of metabolism), cystic fibrosis, Tyrosinemia, Moriquo syndrome
- If both parents are carriers for cystic fibrosis, the fetus can be tested using CVS or amniocentesis.

Chorionic Villus Sampling (CVS)

- CVS is biopsy of chorionic villi performed for prenatal diagnosis of genetic disorders.
- Usually performed b/w 10-13 wks.
- Limb reduction defect are a/w early CVS.
- Rh-negative women should receive Anti-D immunoglobulin 50 mg i/m post procedure.
- Needs amniocentesis for confirmation.

→ NTDs are not diagnosed by CVS prenatally.

→ Triple test usually performed between 15-18 wks.

→ Ultrasound for detection of congenital anomalies is performed b/w 18-20 wks.

Amniocentesis

- Indications: Chromosomal & fetal disorders.
- Usually performed b/w **15-20 wks** (2nd trimester).
- Early amniocentesis is can be performed b/w **11-13 wks**. It is a/w higher rates complications than usual 2nd trimester amniocentesis.
- Important complications are:
Clubfoot, fetal loss, cell culture failure requiring repeat procedure.

Fetal Blood Sampling (Cordocentesis)

- Also k/as PUBS (percutaneous umbilical bld sampling)
- Indication is assesment and t/t of confirmed red cell or platelet alloimmunization and evaluation of **non-immune hydrops**.
- C/b used for genetic analysis when CVS or amniocentesis results are confusing.

Fetal Tissue Biopsy

- Sometimes prenatal d/g can only be accomplished by direct analysis of fetal tissue obtained by USG guided biopsy

- This technique has been used for muscle biopsy to diagnose muscle dystrophy or mitochondrial myopathy. A skin biopsy has been used to diagnose **epidermolysis bullosa**.

→ Prenatal d/g using CVS or amniocentesis is not possible for muscle dystrophy, mitochondrial myopathy, or epidermolysis bullosa. Biopsy is required.

→ NTDs are not diagnosed by CVS prenatally

ANTENATAL ULTRASOUND

- Role of USG in computing gestational age gives best predictive value in first trimester.
- For determination of gestation age in 1st trimester: - CRL is used
- Determination of gestation age/ fetal maturity in IInd & IIIrd trimester --- **BPD** is used upto 28wk.
- FL (femur length) is more reliable USG parameter for fetal age during later gestation.
- AC (Fetal Abdominal circumference) is the single best USG parameter for assessment of IUGR.

Imp. transvaginal USG finding in 1st trimester

Sign	Seen earliest at by TV-USG	Inference
1. Intrauterine GS	When β-hCG level >1000-1200 mIU/ml	Normal intrauterine gestation
<ul style="list-style-type: none"> Choriodecidual thickness Double decidual sac sign (gestational sac + yolk sac) Fetal pole, cardiac activity CRL 5 mm 	4 wk 5 wk 6 wk	
2. Pseudogestational sac	In 1st trimester	Ectopic pregnancy
3. ↑ nuchal-fold thickness >3 mm	In 1st trimester.	Trisomy 21, 18, 13, Turner syndrome

→ Double decidual sign' of gestation sac is d/to the interface b/w the decidua and chorion which appears as two distinct layers of the wall of the gestational sac. It indicates normal intrauterine gestation.

→ Transvaginal ultrasound can detect 90% of tubal ectopic pregnancy. The 'double decidual sac sign' differentiates normal pregnancy from pseudogestational sac of an ectopic pregnancy.

PREGNANCY SCALE

Embryonic age

Implantation 6th day -----(It corresponds to the 20th day
of regular menstrual cycle)**0 HOUR FERTILIZATION (= DAY 14 AFTER OVULATION)**

5th day- blastocyst formation

8 days - **pregnancy c/b diagnosed earliest by presence of β -hCG**
(= on 22nd day from LMP or day 8 post ovulation) using
Radioreceptor assay or serum β -hCG9-10 days - Pregnancy diagnosis by +nce of β -HCG
on 25th day using radioimmune assay (urine PT)3 wk (21 days) Fetoplacental circulation established

(LMP is used below)

FETAL DEVELOPMENT

↓

Cardiac pulsations -----

Genotypes, Ovary/ testes distinguishable-----

Intestines in abdomen, finger, toes, skin, nails+

Sex distinguishable externally, penis/ vagina

Radiological e/o fetal skeletal shadow-----

2nd trimester screening for NTDs →

Surfactant synthesis starts, lanugo hairs+

Spinal cord extends to S1-----

Eye opening -----

Fetal weight ~ 1000 gm -----

Term, maturity attained -----

(age from LMP = gestational age)

4 wk

--- Gestational sac by vaginal ultrasound

5 wk

--- Gestational ring

6 wk

--- Gestational sac, yolk sac, fetal poles

} transvaginal probe
can detect all these
events 1-2 wk ear-
lier

7 wk

8 wk

--- Embryonic movements

9 wk

--- CRL for gestational age gives best predictive value

10 wk

11 wk

→ Chorionic villous sampling (CVS)/biopsy

12 wk

--- Uterus at L/o pubic symphysis

14 wk

15 wk

16 wk

--- Quickening starts in multipara
height of uterus midway b/n P.S. & umbilicus

18 wk

→ Quickening starts in primi
Ideal time for USG screening of gross congenital anomaly

20 wk

--- Iron prophylaxis in pregnancy.

22 wk

24 wk

--- Fundal height of uterus at L/o umbilicus

26 wk

→ Universal screening for GDM by GTT

28 wk

→ Prophylactic anti-D to all unsensitized Rh -ve women

30 wk

32 wk

34 wk

36 wk

--- Uterus fundal height at L/o xiphisternum,

37 wk

--- Max^m volume of amniotic fluid

38 wk

--- Engagement in primi

40 wk

--- EDD

42+ wk

--- Post term pregnancy

Neural Tube Defects (NTD)

- Prenatal diagnosis of NTDs
 - ↑ MS-AFP and AF-AFP
 - ↑ Acetyl cholinesterase levels in AF is most specific marker for NTD.
 - ↓ butryl cholinesterase in AF is specific for open NTD (open spina bifida).
 - 1st trimester USG - absent skull vault in anencephaly
 - 2nd trimester USG - splaying of spine, lemon sign, Banana sign
- Anencephaly is the m/c NTD (incidence is 1:1000). It is the earliest (first) detectable congenital anomaly by USG. It can be detected by sonologists as early as 12th wk by TVS (10-14 weeks range) of gestation.
- Antenatal folic acid supplementation is useful in preventing NTD.

Down Syndrome

- Antenatal predictors
 - ↑ nuchal fold thickness (Nuchal translucency)
 - ↓ Femur length.
- Levels of β-hCG and inhibin are ↑ed while UE3, AFP ↓ed.

Assessment of fetal maturity

- Date of LMP provides the most accurate means of computing gestational age of fetus (human gestation averages 280 days)
EDD → (9 calendar months + 7 days) from 1st day of LMP
- Uterine size : Height of fundus from pubic symphysis can provide an estimate of gestation (+ 4 weeks). It is ~20 cm at 20 weeks, 28 cm at 28 weeks in absence of obesity, hydramnios, fibroids, twins etc. (unreliable after 28 weeks)

Radiological examination

Distal femoral epiphysis is usually present by 36 weeks and proximal tibial epiphysis by 40 weeks of gestation. Therefore, the absence of distal femoral epiphyses indicates prematurity and the presence of proximal tibial epiphyses connotes maturity.

Fetal lung maturity

- Bedside screening test is **Bubble stability/shake test**.
- Other simple tests are -
Amniotic fluid optical density at 650 nm,
AF L/S ratio >2, creatinine > 2mg (37wk+)
Nile blue sulphate test in amniotic fluid

- Estimation of phosphatidyl glycerol or phosphatidyl choline in amniotic fluid especially in mother with DM is the most reliable test to assess fetal lung maturity.
- Critical ratio of lecithin: sphingomyelin in newborn of diabetic mother (IDM) is 3.5

AMNIOTIC FLUID (AF)

- Volume is maximum b/w 34-36 weeks
50ml (12wk) → 400 ml (20 wk) → 1000 mL (36-38 wk) → **600-800 ml** (at term) → 480 ml (at 42 wks) → 250 ml (at 43 wks) → 160 ml (at 44 wks).
- Source: Mixed maternal & fetal origin (main source of amniotic fluid AFP is fetal urine)
During the first half of pregnancy (or *first trimester*) : Large component of AF is derived from water transport across skin. Horny layer of epidermis is absent before 20th week.
2nd + 3rd trimester : Fetal urine (fetal kidney origin), fetal lungs, amnion
- AF is absorbed by fetal swallowing + GI absorption, fetal lung absorption & clearance by placenta.
- In antenatal ultrasound AFI should be >9 near term and largest pocket should be >3cm.

- AFP level

Maternal serum	30 ng/ml	30-32 nd wk
Amniotic fluid	20,000 early	2nd wk
Fetal plasma / serum	3,00,000	14-15wk (maximum)

- Fetal urine is major source of AF in second half of gestation
- Fetus begins to swallow AF at 8-11 wks of gestation.
- Presence of acetylcholine esterase in amniotic fluid is specific for the d/g of open NTD (Open spina bifida)
- Nile blue sulphate test in AF is done to see fetal lung maturity.

Abnormal colour of amniotic fluid

- Meconium stained / --- Fetal distress
greyn/ pea-souped (d/to bile pigments)
- Golden (d/to ↑↑ bilirubin) --- Rh-incompatibility.
- Greenish yellow (saffron) --- In post maturity.
- Dark coloured/ Tobacco juice coloured --- IUD
- Dark coloured, containing blood --- in concealed abruptio placentae

HYDRAMNIOS

Properties	Oligohydramnios	Polyhydramnios
Amt of AF	<100 mL	>2000 mL
USG Criteria	AFI ≤5cm or <5% for gestational age	Largest pocket ≥8cm
Associations	Breech	Maternal DM, preterm labour
Cause	Potter syndrome (renal agenesis) Urinary tract obstruction Placental insufficiency with IUGR	Obstruction to g.i.t (eg. Esophageal atresia) 100% Anencephaly (in 50%), microcephaly, encephalocele Open spina bifida Maternal DM, Rh-isoimmunization Hydrops fetalis Preterm labour Infections: Rubella, syphilis, toxoplasmosis

→ Polyhydramnios at 20 weeks may be d/to --- Congenital diaphragmatic hernia.

PLACENTA

- Develops from --- chorion frondosum
- Human placenta is product of conceptus. It is discoidal, hemochorial, deciduate, chorioallantoic placenta. Disc is circular with a diameter of 15-20 cm, weight is 500 gm and its ratio with fetal weight is 1:6 at term.

Types

Extrachorial P~

- Circumvallate** : Placenta in which chorionic plate is smaller than basal plate
- Circummarginate** : ↑rate of prematurity, PPH, polyp formation & subinvolution

Succenturiate P~

- Has accessory lobes in membrane away from main placenta.
- They are connected with main body by large vessels. If succenturiate lobe is left within the uterus after main body has delivered risk of ↑ PPH.
- If no blood supply in S~ then it is called vasa spuria (placenta spuria)
- Complication: Vasa previa (blood loss of fetal origin)

Membranous P~

- Has functional villi covering all the fetal membranes (it develops from chorion laeve in addition to chorion frondosum)

Velamentous placenta

- Cord is attached to the membranes (not with placenta)
- Branching vessel traverse a long distance. Blood vessels are prone to leak at internal os, in front of presenting part k/as *VASA PREVIA* in which blood is of fetal origin.
- It may result in fetal exsanguination & even death.

Battledore P~

- Cord is attached to the margin of placenta
- Increased chances of cord compression are there if implantation occurs in lower segment

Fenestrated P~:

- Central portion of placenta is missing

Placenta accreta:

- Condition in which Nitabuch layer b/n placenta & decidua (usual plane of cleavage) is - nt & villi is attached to myometrium
- If villi penetrates into muscle bundles → placenta increta
- If villi penetrate up to serosa → placenta percreta (if placenta grows through myometrium)
- It is more common in women who have uterine scars (previous C.S.)
- Doppler ultrasound is helpful in d/g. D/g is confirmed only after delivery.
- Manual removal (sometimes vigorous) required, ↑ risk of PPH/ perforation / uterine inversion.
- In total P~ : Hysterectomy is advised in parous women, conservative attitude in young + inj Methotrexate is given (Umbilical cord is cut as high as possible leaving behind the placenta)

Large placenta is seen in

- Polyhydramnios,
- Nephrosis (hydro-/pyo)
- CMV, Toxoplasma, Syphilis,
- Rh incompatibility,
- DM

Risk factors for placenta previa

- Prior surgery (LSCS)
- Uterine curettage
- Endometriosis
- Age > 35 years, Increasing parity

Hypertension is a/w placental abruption.

Blood loss of fetal origin is seen in

1. In vasa previa (APH may occur, singer's test +ve)
2. In velamentous placenta

Decidua and Villi

	In uterus	Cast shed P/V
• In Normal pregnancy	Vascular villi+	Decidua capsularis & vera
• In Ectopic pregnancy	Decidua in uterus	Decidua Vera but no chorionic villi
• In Blighted Ovum & H. mole	Avascular villi+	

ANTENATAL ASSESSMENT OF FETAL WELL-BEING

Contraction Stress Test /OCT (Oxytocin Challenge Test)

- Earlier called as OCT
- Useful in assessment of integrity of utero-placental unit.
- Contractions were induced using i/v oxytocin or nipple stimulation, and FHR response is recorded using standard monitors.
- Early decelerations are d/to compression of head. A/w fetal bradycardia. Can be prevented by Atropine.
- Variable deceleration is d/to cord compression.
- Late deceleration is d/to utero-placental insufficiency (a/w pre-eclampsia, chronic hypertension, abruption, IUGR). A/w fetal hypoxia and acidosis. Imminent delivery is required.
- Interpretation of CST
 1. *Negative CST or OCT* : No late or significant variable decelerations. Indicates healthy fetus
 2. *Positive (abnormal) OCT* : Uniform repetitive late **FHR decelerations** following >50% contractions. It indicates utero-placental insufficiency
 3. *Equivocal-suspicious CST* : Intermittent late or significant variable decelerations

4. *Equivocal- hyperstimulatory CST* : FHR decelerations in +nce of frequent contractions (<2 min interval) or lasting >1.5 min

5. *Unsatisfactory CST* : <3 contractions in 10 min

- If OCT shows **persistent late deceleration**.
AF L/S ratio >2 → It indicates fetal maturity → baby should be delivered immediately
AF L/S ratio <2 → Wait for satisfactory estriol levels/fetal maturity

• C/ind to OCT

Placenta previa, PIH., H/o Previous LSCS, High-risk conditions for preterm labour [Twins, AROM, Incompetent cervical os]

[mnemonic : TRIPP]

Non-Stress Test (NST)

- Test of fetal condition.
- Most widely used primary testing method for assesment of antenatl fetal well-being. It has also been incorporated in bio-physical profile.
- Based on **FHR acceleration** in response to fetal movement (percieved by mother) as a sign of fetal health.
- Interpretation of NST
 1. *Normal NST* : >2 accelerations that peak at >15 bpm above baseline, all occuring within 20 min of beginning of test.
 2. *Abormal NST* :
 - Silent oscillatory pattern**: Omnious
 - Terminal CTG**: Baseline oscillations of <5 bpm, absent accelerations or late decelerations with spontaneous uterine contractions
- Variable FHR deceleration during NST do not indicate fetal compromise
 - *Fetal scalp blood sampling to assess fetal hypoxia is an obsolete practice now a days.*
 - *These days only NST is used. If NST is non-reassuring then decide to deliver the baby immediately.*

Intrapartum CTG

- Cardiotocograph (CTG) is a non-invasive and quick method to assess fetal well-being during labour (intrapartum).
- Interpretations
 1. Baseline FHR
 - 110-160 (A sustained rise in FHR >160 bpm is fetal tachycardia while a sustained fall in FHR <100 bpm is fetal bradycardia. NOT applicable in preterms)

2. Long term variability

5-25 bpm (taken over 1 min over the most reactive part of the record with a stable baseline)

3. Unreactive/ flat trace

Loss of normal long-term variability

4. Acceleration

Rise in FHR > 15 bpm for > 15 sec

5. Deceleration

Fall in FHR > 15 bpm for > 15 sec

Early D~ are those where lowest point of the FHR occurs within 20 sec of the peak of contraction

Late D~ where lowest point of the FHR occurs > 20 sec of the peak of contraction there must be 3 or more such decelerations following consecutive contraction. Late D~ are ominous.

• FHR features categorization

Feature	Baseline (bpm)	Variability (bpm)	Deceleration	Accelerations
Reassuring	110-160	>5	None	Presence of > 15 bpm with movements or contractions
Non-reassuring	100-109	<5 for 40-90 min	Early or Prolonged d~ < 3 min	Present but not well defined. Baseline is flat
Abnormal	<100 or >180	<5 for >90 min	Persistent late d~ or Prolonged d~ of > 3 min	—do—

- CTG traces are normal if all 4 features are in reassuring category and pathological if >2 non-reassuring category and >1 in abnormal category.

→ Late decelerations are significant and ominous sign

→ Baseline FHR >160 is not applicable to preterms.

→ Sinusoidal pattern is stable baseline FHR with fixed baseline variability without acceleration. Seen in Fetal anemia, Feto-maternal h'age (Rh-incompatibility), fetal hypoxia, narcotics abuse.

BIOPHYSICAL PROFILE [Manning score] -

- Includes 5 parameters

1. NST

2. Fetal breathing

3. Fetal tone

4. Gross fetal movement (limb movements)

5. Amniotic fluid volume (adequate amniotic fluid pockets)

- B~ is the non invasive & most reliable parameter of fetal well being
- Each variable has 2 points. Highest score is 10

Modified Biophysical profile

- Includes combination of observations of 2 indices
 1. An index of acute fetal hypoxia --- NST with VAST (variable acoustic stimulation test)
 2. An index of chronic fetal problems—Amniotic fluid volume (AFI). AFI < 5 cm is considered abnormal.
- It is the only parameter used to assess fetal well being in well equipped centres.

DOPPLER VELOCIMETRY

- Doppler ultrasound is a non-invasive method to assess blood flow through placenta after 20 wks.
- Blood flow across 3 fetal circuits is measured --- umbilical artery, MCA (middle cerebral artery), and ductus venosus.
- Umbilical artery S/D ratio (systolic: diastolic ratio) is considered abnormal if it is >3 after 30 weeks of gestation Seen in IUGR.
 - High resistance in the umbilical artery is c/by a fall in diastolic flow and an absence/reversal of diastolic flow.
 - Absent end diastolic flow in umbilical artery is an indication of induction.
 - Reversal of end diastolic flow in umbilical artery is more ominous and is an indication of termination of pregnancy (delivering the baby) because it indicates imminent fetal death.
- In uterine artery the presence of a diastolic notch is a normal phenomenon up to 26 weeks of gestation. Presence of a notch after 26 weeks is a bad indicator leading to hypertensive and SGA complications. Persistence of a notch after 26 weeks indicates vasospasm. High resistance in uterine artery in doppler is a/w complications like risk of abruption (abruptio placentae), pre-eclampsia, or IUGR.

LABOUR EVENTS

Normal Labour

- Duration of first stage in primi is 12-14 hours and in multipara is 6-8 hours.
- Rate of Cx dilatation is 1-1.2 cm/hr in primi and 1.5 cm/hr in multigravida
- Sequence of labour events

1. <u>E</u> ngagement	2. <u>D</u> escent
3. <u>F</u> lexion	4. <u>I</u> nternal rotation
5. <u>C</u> rowning	6. <u>E</u> xternal rotation
7. <u>R</u> estitution	8. <u>E</u> xpulsion

[Mnemonic : EDFICERE]

→ Expulsion of placenta is seen in 3rd stage of labour.

→ Physiological chills in labour are seen in - 4th stage.

- Partogram**
Composite graphical record of progress of labour. It includes uterine contractions, cervical dilatation in time scale, descent of fetal head.
- Bishop's score**
Includes dilatation, effacement, consistency, position of cervix & station of head.
Favorable score 6-13 [>6 indicates that labour has begun]
- Cervicograph**
It shows dilatation of Cx and descent of presenting part against duration of labour. Labour is considered abnormal if cervicograph crosses alert line & falls towards action line.

Engagement

- When in greatest horizontal plane, biparietal diameter passes pelvic brim, it is k/as engagement of head
- In primigravida - Occurs before onset of labour (after 37 completed weeks or during 38th week)
- In multipara - Late in 1st stage after rupture of membrane.
- M/c engaging diameter - Sub-occipitobregmatic (in vertex Presentation)
M/c lie - Longitudinal (99.5%).
- Diameter of engagement in
Brow presentation - Mentovertical
Face presentation - Sub- mentobregmatic, or SMV
- Largest/ max^m fetal diameter is mentovertical (>14 cm.).
- Head never engages if presenting diameter is mentovertical (>14 cm.)

- Delivery is possible only if presenting diameter is mentoanterior and baby is small.

Prolonged labour & Latent phase

- Labour is called **precipitate** when the combined duration of 1st and 2nd stage is < 2 h.
- Arrest of labour** : When there is no further dilataⁿ of cervix for a min^m period of 2 h in active phase.
- PROLONGED LABOUR** : When the duration of labour exceeds $>18-24$ h or fails to make changes in dilation or effacement. Normal rate for--
Cervical dilation : Primi 1.2 cm / hr, in multi 1.5 cm / hr
Descent @ 1 cm / hr in primi & 2 cm / hr. in multigravida
- Prolonged 1st stage : 2 components
 - (a) *Prolonged latent phase* is one which exceeds >20 h in a primi and > 14 h in a multigravida.
 - (a) *Prolonged active phase* is termed when there is rate of Cx dilatation is <1.2 cm/h in a primi or < 1.5 cm/hour in a multigravida.
- Prolonged second stage : when its duration is >2 h in a primi and > 1 h in a multigravida.
- Prolonged rupture of membrane :
Time b/w ROM and delivery is >24 h.
- PROM** : Pre-labour Rupture of Membranes.
ROM preceding the actual onset of labour pains. ROM is usually 24 hrs prior to the onset of labour.
- PPROM** : Preterm Premature Rupture of Membranes.
If PROM occurs before 37 weeks.

Preterm labour

Labour onset <37 th completed week (<259 d) from LMP

- Very early (extreme preterm) < 32 weeks
 - Early preterm 32 - 33.6 weeks
 - Late preterm 34 - 36.6 weeks
- Minimum period for considering fetal viability is --- 28week (1000gm) in India.
 - Postmaturity /Post-term labour is > 294 d (>42 wk). But there are variable criterias.
 - Post dated pregnancy is >40 weeks pregnancy.

Cord Prolapse

- Cord prolapse** : The umbilical cord lies alongside or below the presenting part after the rupture of membrane.
- Cord presentation** : The umbilical cord lies alongside or below the presenting part with the membranes intact.

	Membrane	Cord
Occult prolapse	+/-	not felt
Cord prolapse	- nt	felt
Cord presentation	+	felt
Compound presentation		head/hand

→ C.S. is done when vaginal delivery is unsafe (malpresentation, big baby, CPD, malposition) and Cx dilatation and descent of head cross alert line.

→ Braxton Hicks contractions are seen in pregnancy, hematometra, subserous/submucous fibroid.

Active m/m of 3rd stage of labour include

- Use of oxytocics e.g. Methargin (methyl ergometrine)/ syntometrine, oxytocin, prostaglandins. Uterotonic e.g. oxytocin (syntocinon) 5 units i.m. or slow i/v infusion c/b given within 1 min. of birth of baby/with the delivery of anterior shoulder.
- Clamping and cutting cord soon after births.
- Applying controlled cord traction to deliver the placenta once separation has occurred (**Bandt-Andrew's method**).
- Gentle uterine massage c/b given.
- *Crede's method* is applying fundal pressure with cord traction. Fundal pressure is not included in active m/m of 3rd stage labour as it may lead to inversion of uterus.

M/m of preterm labour includes

- **ANS (Antenatal steroids)** :
Use of glucocorticoids if pregnancy is <34 weeks
Betamethasone 12 mg 24 hr apart, 2 doses (or dexamethasone 6mg 12 hr apart, 4 doses) are given to mother for fetal lung maturity. Known to ↓ the incidence of HMD, IVH, NEC, PVL. [Betamethasone is better]
- Asymptomatic bacteremia should be treated with antibiotics. Antibiotics can also be given after membrane rupture to prevent neonatal group B streptococcal infection.
- <34 weeks pt not in advanced labour, tocolytics c/b used for short term. Simultaneously fetal lung maturity is achieved by steroid therapy
- 34 weeks or + pt is monitored for labour progression and fetal well being.

Anatomical features of different pelvis

	Inlet	Outlet(Sub pubic angle)	Outcome
Gynaecoid M/c type (50%)	Rounded	Wide	Vaginal delivery is possible without any difficulty
Anthropoid 25%	AP-oval shape	Slightly narrow	Direct OAP or OPP Non-rotation is common Face to pubis delivery
Android 20%	Triangular	Narrow	Difficult delivery with delay in engagement DTA & perineal injuries
Platyploid (Rarest type)	Transversally oval	very wide	No difficulty in VD Ant. rotation occurs late

Attitude of head and Engaging Diameters

Presentation	Attitude of head	Engaging(AP) diameter of fetus
Vertex	Complete flexion	SOB (sub-occipito bregmatic)
	Incomplete "	SOF
	Deflexion "	OF (occipitofrontal)
Brow	Partial extension	MV (mentovertical)
Face	Incomplete extension	SMV
	Complete extension	SMB

Pelvic inlet (AP diameters of pelvis)

	Diagonal conjugate (DC)	True conjugate (Anatomical/AP)	Obstetric conjugate
1. Distance from midpoint of sacral promontory to---	Lower border of S.P	Upper border of SP	Midline projection of SP
2. Measurement	12 cm	11 cm (DC-1.2 cm)	10 cm (DC-1.5cm)
3. Measured by	Pelvimetry	Conjugate vera	

- *Obstetric conjugate measures 10 cm (smallest AP diameter). Calculated by subtracting 1.5 –2 cm from DC*
- *Osteomalacic pelvis – Shape at inlet become triradiate.*
- *Rachitic pelvis – Shape of inlet become reniform.*

Transverse diameter of pelvis

- At pelvic inlet → 13 cm
- At pelvic cavity → 12 cm
- At obstetric outlet → 10.5 cm (Bispinous, b/n ischial spines)
- At anatomical outlet → 11 cm (Intertuberous, b/n ischial tuberosities)
- At midpelvis → 10.5 (Bispinous)

→ Bispinous diameter is narrowest transverse diameter of pelvis. It lies b/w two ischial spines.

Important transverse diameters of fetal skull.

- Biparietal 9.5 cm
- Superior sub-parietal 8.5 cm
- Bitemporal 8 cm
- Bi-mastoid 7.5 cm

FETAL MALAPOSITIONS

Occipitoposterior Position (OPP)

- The occiput is placed posteriorly over the sacroiliac joints or directly over sacrum.
- In favourable circumstances (90%) occiput rotates anteriorly and follows the course like (OAP) position.
- In unfavourable circumstances (10%) it can be
 - Incomplete forward rotation --- DTA (deep transverse arrest)
 - Non rotation --- oblique posterior arrest
 - Mal rotation --- persistent occipitoposterior position (POPP) or face to pubis delivery.

→ Normal vaginal delivery is not possible in persistent mento-posterior

→ Face to pubis delivery occur in persistent occipito posterior or occipito sacral position.

BREECH

Frank breech (extended breech)	<ul style="list-style-type: none"> Maximum arrest Least cord compression (0.5%) Best P/g Seen in primi ECV fails Engagement earliest
Complete/flexed breech	<ul style="list-style-type: none"> M/c type of breech Cord compression (5%) Seen in multipara ECV is successful

Footling breech

- Max^m (15%) cord compression
- Worst p/g
- Elective CS is indicated
- Late engagement

→ In knee presentation thighs are extended but knees are flexed (knees presenting at brim)

→ Cord prolapse is maximum in transverse lie > footling breech > complete breech > frank > Brow (Least)

→ Maneuver used for delivery of aftercoming head in breech --- Mauriceau smellie veit maneuver

Shoulder Dystocia

- Risk factors are : Fetal macrosomia, obesity, diabetes, postmaturity, multiparity, anencephaly, fetal ascites (weight gain), midpelvic instrumental delivery
- M/m steps
 - Suprapubic pressure → Mc Roberts maneuver → Wood's corkscrew's manœuvre → Extraction of posterior arm → cleidotomy
 - (In Mc Roberts maneuver hip is flexed against mother's abdomen which may lead to injury to lumbosacral trunk)
 - Fundal pressure is avoided** as it causes further impaction of the shoulder. Moreover it causes neurological and orthopaedic damage. Traction over baby's head is also avoided. If it is a b/L S~ then proceed for LSCS directly after doing Zavanelli's manoeuvre.
- A/w prolonged labour.
- C/c are : Fetal clavicle/ humerus #, brachial plexus injury. Maternal c/c are: perineal tears, h'age, uterine rupture

Constriction ring Vs Retraction ring

	Constriction Ring (Schroeder's)	Retraction Ring of Bandl's
Cause	Inco-ordinate uterine contractions (Undue irritability of uterus/ oxytocics, PROM)	D/to tonic uterine contraction & retraction following <u>obstructed labour</u>
Location	Static at junction of upper and lower segment	Always starts at junction of upper and lower segment and progresses upward
P/A	Uterus is non-tender, fetal parts are felt. Ring is not felt abdominally	O/E <u>uterus tender</u> , we can not feel fetal parts & <u>FHS -nt</u> , Ring is felt as oblique groove
P/V	Ring is felt usually above the head	Ring is not felt
C/c	Less	<u>Rupture of uterus is common</u>

HEMORRHAGE IN PREGNANCY

- Bleeding in the first trimester of pregnancy is quite common and may be d/to the following:
 - Miscarriage (pregnancy loss)
 - Ectopic pregnancy (pregnancy in the fallopian tube)
 - Gestational trophoblastic d/s
 - Implantation of the placenta in the uterus
 - Infection
- Bleeding in the late pregnancy (> 20 weeks) may be d/ to the following:
 - Placenta previa (placenta is near or covers the cervical opening)
 - Placental abruption (placenta detaches prematurely from the uterus)
 - Idopathic /unknown cause

ECTOPIC PREGNANCY

- M/c site is fallopian tube (in 95%) --
 - Ampulla (55%) : M/c site in FT
 - Isthmus (25%) : *disturbance or rupture earliest because it is the narrowest part of the tube.*
 - Infundibular (18%)
 - Interstitial (2%) : (pregnancy longest) may continue for 3-4 month.
- M/c cause is PID
- Decidua vera is shed
- In ectopic pregnancy serum β -HCG are positive in 100% cases, while in urine, pregnancy test is +ve only in 50%.
-ve β -HCG level in serum excludes the d/g of ectopic
- OCPs are protective against ectopic, however IUCD use, POP & Post coital estrogen pills increases the incidence of ectopic pregnancy by decreasing tubal motility.
- Triad:

Amenorrhoea + abdominal pain (m/c symptom) + vaginal bleeding.
- Spiegelberg's criteria : Helps to identify the ovarian pregnancy from other ectopics:
 - The gestational sac is located in the region of the ovary.
 - The gestational sac is attached to the uterus by the ovarian ligament.
 - Ovarian tissue is histologically proven in the wall of the gestational sac.
 - The oviduct on the affected side is intact (this criterion, however, holds not true for a longer ongoing ovarian pregnancy).

On USG

Tubal ring sign (Bagel sign/) along with empty gestational sac = pseudogestational sac is seen.

D/g

Based on Clinical triad + fluid in cul de sac which fails to clot + positive pregnancy test & abnormal pelvic mass.

M/m of Ectopic

The principle in the m/m of acute ectopic is **resuscitation and laparotomy** & not resuscitation followed by laparotomy." If the patient is in shock, immediate resuscitation & M/m of shock is required, simultaneously laparotomy is also done (quick in quick out).

T/t of Unruptured tubal ectopic

Expectant m/m indicated if	<ul style="list-style-type: none"> • ↓ ing hCG titre • Ectopic mass < 4 cm • No evidence of bleeding/ rupture
Medical m/m	<ul style="list-style-type: none"> • Salpingocentesis (lysis of ectopic) <ul style="list-style-type: none"> - Mtx, KCl, - PGF_{2α} - Hyperosmolar glucose/actinomycin Pt must be stable, tubal diameter should be < 4 cm & absent fetal cardiac activity & β hCG levels < 10,000 are required for salpingocentesis
Conservation surgery	<ul style="list-style-type: none"> • Laparoscopically /micro surgical laparotomy. • Linear salpingostomy. • Segmental resection (for isthmic E-). • Plucking out from distal tube/ milking of tube (for distal ampullary/fimbrial pregnancy)

→ Salpingectomy is TOC when whole of the tube damaged.

→ TOC for chronic ectopic/uncomplicated suspected ectopic → Hospitalize & do laparotomy. Diagnostic laparoscopy c/b done (removal of pelvic hematocoele if present & salpingectomy)

PLACENTA PREVIA (PP)

- It is a leading cause of antepartum haemorrhage (vaginal bleeding).
- Risk factors : Prior surgery (LSCS), previous uterine curettage, endometritis, ↑ing maternal parity/ age (>35).
- PV examination is not done routinely in every case of PP, it is indicated only if --- USG is not available, If disparity exists b/w cl/f+ USG report, and for minor degree of PP (type I, II anterior)
- PAGE classification is used for abruption placentae.

M/m

- Expectant m/m of placenta previa includes ---
MacAfee and Johnson's regimen, which consist of complete bed rest, tocolytics, steroids to enhance lung maturity of baby, Anti-D if mother is Rh-ve. Criteria to apply this regimen are

- No fetal distress
- Mother should be hemodynamically stable, FHS good
- Pregnancy <36-37 wk

In these conditions conservative m/m is done.

- Active m/m (termination of pregnancy by LSCS) in case of
 - Severe continuous bleeding
 - Pregnancy > 37 wk
 - Patient in labour
 - Fetal malformation/ dead fetus

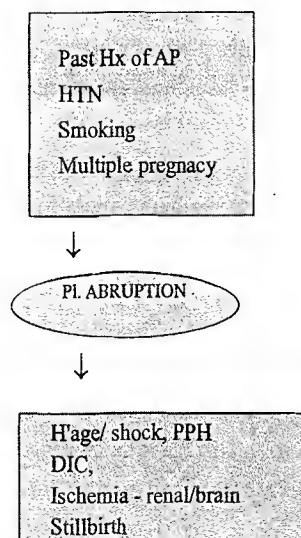
- Placenta previa grade IIb, III & IV --- C.S.
 Grade I, IIa without significant bleed--- Vaginal delivery

	Placenta praevia	Abruptio placentae
1. Also k/as	Warning h'age, (Fresh revealed bleed)	Accidental h'age (Usually concealed or mixed bleed)
2. Risk factors	Previous Sx (C-section, curettage), multipara	Smoking
3. A/w	Malpresentations like breech, folate deficiency	
4. Placenta is lying in	Lower segment (low lying)	Upper segment
5. Uterus is	Soft, relaxed, non-tender	Contracted, tender, rigid, tense
6. Bleeding is	Painless, causeless, recurrent	Continuous with features of toxemia
6. Fetal effects	H'age is rarely fatal	Fatal h'age → Hypotension/shock → Fetal distress → Fetal demise (not FHS)
7. Dx	Ultrasound	Clinical
4. T/t	Conservative, P/V in OT → Em. CS if needed	Stabilize, t/t of shock → Deliver the baby

PLACENTAL ABRUPTION (AP)

- Placental abruption is the premature separation of a placenta from its implantation in the uterus. The larger the area that detaches, the greater the amount of bleeding.
- Incidence - 1 in every 120 births.

- Associations & complication



- Can cause renal failure.

PPH (Post - Partum Hemorrhage)

- Primary hemorrhage occurs within 24 hour & secondary hemorrhage after 24 hrs and within puerperium (delayed/ late puerperal hemorrhage)
- M/c cause is atonic uterus - uterus is flabby and becomes hard on massage.
- Risk of PPH increases with -
 APH (HTN), Twins, hydramnios, grand multipara, H/O previous 3rd stage complications, severe anemia.
- M/m
 - IV methergine/ ergometrine
 - If patient is in shock, resuscitation is the first priority. Start DNS drip and arrange BT
 - Massage the uterus to make it hard in case of atonic uterus.
- Drugs used to treat PPH
 - Oxytocics are used, that bring about contraction of uterus
 - 1. Oxytocin
 - 2. Ergometrine (ergonovine), methylergotamine/ Methergine (Remember that these drug are contraindicated in a patient with RHD, preeclampsia, chronic hypertension and after the delivery of twin₁ in multiple gestation)
 - 3. Prostaglandins:
 - PGF_{2α} (Carboprost)
 - PGE₁ (misoprostol).

- Surgical m/m of uterine atony

- Conservative : Compression sutures (B-Lynch/ Chao's multiple square sutures)

2. Sequential devascularization of uterus
3. Hysterectomy is indicated if all other measures fail/ life threatening situation/ no future pregnancy plan.

MULTIPLE GESTATION, TWIN PREGNANCY

- Multiple pregnancies (> 2 fetus in uterus) are a/w following complications in ↑ed frequency.
 - Hyperemesis
 - Anemia
 - Hydramnios
 - APH
 - Pre-eclampsia (PIH)
 - Malpresentation (more common in 2nd baby)
 - Preterm labour (but not postdated pregnancy)
 - Fetal congenital anomalies (Risk ↑es twice than singleton pregnancy).
- Multiple birth are commonest among Negros (in Nigeria).
- Incidence in India is 1 in 80. Incidence is increasing bec/ of use of ovulation induction drugs
- **Hellin's rule** states mathematical frequency of multifetal pregnancy which is for twins 1 in 80, for triplets 1 in 80² for qudrilets 1 in 80³ and so on
- Chorionicity is determined by USG as early as 1st trimester.
 - Twin peak sign suggest dichorionicity
 - Membrane thickness of <2 mm and T signs suggest monochorionicity
 - Twins of opposite sex are almost always dizygotic but twins of same sex does NOT exclude dichorionicity
 - Confined blood 'Chimerism' is most frequently seen in Monochorionic and diamniotic twins. **Monoamniotic dizygous twins are common after IVF.**
- Majority of conjoint twins are thoracopagus.
- *C/c of twin pregnancy* :
 - Maternal : PPH, APH, preeclampsia, hydramnios
 - Fetal : Prematurity, IUGR, PROM, prolapse of cord, , abortion, vanishing twin, discordant twin, *Twin to twin transfusion syndrome* (seen only in monozygotic-monochorionic twins in which one twin looks plethoric d/to polycythemia and another looks pale d/to anemia).
 - Twin revrsd arterial perfusion (TRAP) sequence is a rare but serious complication of monochorionic, monozygotic multiple gestations → acardiac twin.

- *Indications of abort in CS pregnant pregnancy*
 - First twin is non-vertex
 - First twin with cord prolapse
 - 1 fetal demise + 1 live fetus
 - Monoamniotic twins, conjoint twins, chronic twin-twin transfusion syndrome, previous LSCS, severe IUGR
- Multiple pregnancy reduction is done by USG guided fetal intracardiac injection of KCl.

ABORTIONS, MTP

- **MTP act**: Only female's consent is required to perform an MTP under MTP act 1971. The confidentiality has to be maintained.
- Require single doctor opinion (if ≤12 wk) & 2 doctors opinion if (>12 wk).
- Menstrual regulation is used upto 7 weeks.
- S & E (Suction and evacuation) is most effective method of termination upto 12 weeks of pregnancy
- Latest medical method of 1st trimester MTP :

Oral 600 mg mifepristone single dose f/b 400 mg of misoprostol at 36-48 hours. It is effective upto 49-63 days

Types of abortion

Type	Bleeding	Uterine size	Cervical Os
• Threatened	Slight, Painless	= to GA	Closed
• Inevitable	Painful	= /< than GA	Dilated
• Incomplete	Profuse	< than GA	Dilated
• Missed	Pregnancy symptoms ±	< than GA	Closed

[GA = Gestational age]

- If threatened abortion is a/w CL cyst (adnexal mass) lower abdominal. pain is usually present.
- Endocarditis developing after septic abortion, usually involves tricuspid valve.

Recurrent miscarriages

- Defined as the loss of three or more consecutive pregnancies, affects 1% of couples trying to conceive.
- *Causes of recurrent, habitual abortions are*
 - Anatomical defect : Septate uterus
 - Luteal phase defect

- Parental cytogenetic(chromosomal) anomalies
- Balanced chromosomal translocations
- Lupus anticoagulant
- Cervical incompetence
- Hypothyroidism

- o M/c anatomical/uterine cause of recurrent miscarriage is → Septate uterus.
- o Tests for recurrent miscarriages:
Parental karyotyping,
Lupus anticoagulant, USG abdomen (Rarely/NOT torch)

→ M/c cause of first trimester abortion ---Genetic/chromosomal (parental cytogenetic anomalies) autosomal trisomy (esp. trisomy 16) is commonest chromosomal anomaly encountered.

→ TORCH infection is an important cause of early pregnancy loss but is rarely implicated in recurrent miscarriage.

→ Cervicofetal factors are related to second trimester abortion.

→ M/c cause of 2nd trimester abortions - Cervical os incompetence

→ Parental cytogenetic anomalies are m/c cause of recurrent abortions. Genital tract anomalies are implicated in approx. 24% of recurrent miscarriage

→ Recurrent spontaneous abortions in first trimester occur due to ---Allo-immune causes, antiphospholipid antibodies

VERSION

- o ECV (External Cephalic Version)
 - Indicated in transverse lie (34-36 wks & early labour)
 - Breech (32-34 wks)
 - Chief indication are to convert a breech or shoulder presentation into a vertex (Internal podalic version)
 - ECV is c/ind in severe APH, post CS pregnancy, severe CPD, PIH etc.
- o IPV (Internal version is always always podalic IPV)
 - Performed during 2nd stage after full dilatation of Cx under GA (trans lie of 2nd twin, 2nd fetus of twins)
 - Only Indication now-a-days is 2nd fetus of twins when it is in transverse lie (In shoulder presentation where fetus is small / dead)
 - C/c--- Risk of lower segment uterine rupture, fetal compromise
- o Bipolar version (Braxton Hick's) and EPV are not performed now-a-days.

VENTOUSE/VACCUUM EXTRACTION (VAVD)

- o Designated to assist delivery. Pulling force is applied to drag the cranium. (0.2 - .8 kPa)
- o Indications (3d):
 - DTA with adequate pelvis (e.g. POP)
 - Delay in descent of high head in case of 2nd baby of twins
 - Alternative to forceps
 - Delay in late 1st stage (uterine inertia/cervical dystocia)
 - Applied after Cx dilatation > 7 cm (in contrast to forceps which are applied only in fully dilated Cx 10 cm)
- o C/Ind :-
 - Prematurity - ↑ risk of sub-aponeurotic hemorrhage
 - Face presentation & after coming head of breech
 - Fetal bleeding disorder
(In above mentioned conditions forceps are preferred)

Fetal distress was considered a contraindication in the past but with the advent of newer vacuum machine, vacuum c/b built up in 1 minute and hence vacuume c/b used for fetal distress as well.

- o Pre requisite
 - Cervix should be at least 6 cm dilated
 - Head should be engaged of singleton baby,

FORCEPS

- o Pre requisites (Mnemonic: FORCEPS) :-
 - Fully dilated cx & effaced (~10 cm)
 - Outlet should be adequate (no CPD or obstruction to VD)
 - Ruptured membrane
 - Contractions (uterine) should be +nt
 - Engaged head
 - Presentation should be cephalic
 - Surrounding viscera (bladder & rectum) empty & baby should be alive
- o Anesthesia preferred: pudendal block.
- o Simpson forceps are the most commonly used forceps.
- o Piper's forceps are used to extract aftercoming head of breech. Piper's forceps have a perineal curve to allow application to the after-coming head in breech delivery.

- *Wrigley's forceps* are used in low or outlet delivery when the max^m diameter is about 2.5 cm above the vulva. Now a days these forceps are m/c used in cesarean section delivery where manual traction is proving difficult.
- *Kielland forceps* have small pelvic curve and a sliding lock. Probably the m/c forceps used for rotation.
- *Kocher's artery forceps* are toothed forceps used for rupture of membrane.

NORMAL VIAGINAL DELIVERY (NVD)

Normal Vaginal Delivery is not possible in

- Persistent mento-posterior

Trial of labour is indicated in

Mild CPD but contraindicated in severe CPD, elderly primi, breech & face presentation

	VD is not allowed in	VD is indicated in
• In twins	• Twins with c/c: - Non-cephalic presentation - Monochorionic monoamniotic	• Dichorionic twins with 1st cephalic and II breech presentation
• Malpositions	• Mentoposterior • Transverse lie	• Mento-anterior • Extended (frank) breech
• Others	• HPV infection, Ca Cx stage II, III • Severe IUGR with -nt enddiastolic flow	• CIN, Cancer Cx stage I

CAESAREAN SECTION

Classical or Upper Segment CS

- Classical or upper segment CS is rarely performed now -a- days for limited indications:
Placenta accreta, Ca Cx, high VVF repair, big fibroid on lower segment, placenta previa (III+),
- More chances of rupture of uterus but relatively safer in

placenta previa, Transverse lie .

- Blood loss in an uncomplicated C-section is ~1000 ml.
- Incidence of scar rupture in previous LSCS is 0.1%.

Caesarean Section is Indicated in

Emergency LSCS

Maternal	Fetal
• Previous CS with thin scar	• MSL with fetal distress
• NPOL (Non-progress of labour)	• Acute fetal distress
• Persistent mento-posterior	
• Elderly primi with transverse lie	

Elective LSCS

Maternal	Fetal
• Previous 2 LSCS	• Severe IUGR
• CPD	• Absent liquor (Severe oligohydramnios)
• Severe preeclampsia	• Precious pregnancy
• Transverse lie	
• Primi with breech	
• Prematur breech	
• HIV +ve mother	
• Ca Cervix	
• Previous myectomy	

- LSCS is NOT done for
 - Fetal demise with obstructed labour & shock
(Extraction by destructive procedures) c/b employed.
 - Primi with uncomplicated pregnancy

PREGNANCY & DISEASE

HEART DISEASES IN PREGNANCY

Pregnancy is safe in	- MR - MVP - HOCM - WPW syndrome - ASD, VSD, PDA - AR
Pregnancy is poorly tolerated	- AS - Coarctation of Aorta - TOF - Active Rheumatic carditis
Pregnancy is contraindicated in	- Eisenmenger's complex - Severe AS - Primary pulmonary HTN - Marfan's syndrome with aortic involvement - Severe ms with secondary pulm HTN - CoA with valvular involvement

- MS is the m/c heart d/s met during pregnancy and has the worst prognosis.
- ASD is m/c congenital heart lesion during pregnancy
Termination of pregnancy is considered in --- Eisenmenger's syndrome (Risk of maternal mortality is highest in this condition)
- Appropriate antibiotic prophylaxis is needed for---
 1. Valvular HD
 2. MVP with MR
 3. Idiopathic hypertrophic subaortic stenosis
- There is no role of induction in patient with heart d/s. Induction of labour should be limited to obstetric indications only
- Cesarean Section should be performed only for obstetric indications - tendency of prolonged labour should be curtailed by CS, however in coarctation of aorta elective C.S is indicated to prevent rupture of aorta or mycotic cerebral aneurysm.
- Epidural anaesthesia is preferred.

- Risk of CCF is maximum in --- 2nd stage of labour (bec/ of volume overload). M/c mortality period d/to heart failure.
- 2nd stage of labour is cut short by forceps or ventouse
Corrective cardiac surgery is indicated for - mitral stenosis (valvotomy b/n 14-18 wks)
- Methergine is contraindicated in patient with heart d/s as it causes vasoconstriction and can lead to pulmonary edema

Tuberculosis in Pregnancy

- Common in developing countries.
- If a lady is MT +ve but is asymptomatic, give INH prophylaxis after 1st trimester for 6-9 mo.
- T/t strategy if a lady develops sputum +ve TB in first trimester of pregnancy Start Cat I DOTS
- Avoid streptomycin. (and pyrazinamide if possible)
- Give HRE x2mo followed by HRx 7 mo.

Malaria in Pregnancy

- Common in tropical/developing countries.
- Chloroquine is safe. In resistant cases quinine, artesinate c/b used.
- Effects on mother: megaloblastic anemia, hypoglycemia, metabolic acidosis, jaundice, renal failure, convulsions
- Fetal effects: IUGR, IUFD, preterm labour, abortion.
- Congenital malaria is rare (<5%).

Anemia in Pregnancy

- Acc/to WHO anemia in pregnancy is defined as Hb < 11 gram/dL and Hct < 33%
- Nutritional anemia in pregnancy is d/to iron deficiency, folate deficiency, or combined deficiency (**dimorphic anemia**). Protein deficiency anemia may occur but vitamin B12 deficiency anemia is rare in pregnancy
 - Maternal effects: Uterine inertia, PPH, heart failure, shock, preeclampsia, puerperal sepsis, sub-involution
 - Fetal effects: LBW, IUD, prematurity, PROM, IUGR, behavioural and developmental problems in later life
- Prophylaxis: Supplement FeSO₄ 200 mg (which contains 60 mg elemental iron)
- Indications of BT :
 1. Pregnancy >36 weeks with severe anemia
 2. Refractory to iron t/t
 3. PPH

DIABETES MELLITUS IN PREGNANCY (GESTATIONAL DM)

- Potential candidates for GDM are:
Family H/O DM, previous birth of overweight (macrosomic) baby, Age>30 yrs, Obesity, Unexplained perinatal loss, Presence of hydraamnios or recurrent candidiasis.
- Screening of GDM is done using oral 50 gm of glucose (Glucose chalange test GCT). Performed at 24-28 wk of gestation. Plasma glucose level >140 requires confirmation → glucose tolerance test (GTT) with 100gm glucose.
- Effect of GDM on pregnancy/associations
 - **Maternal:** Abortion, preterm, **polyhydramnios**, prolonged labour, **shoulder dystocia**.
Fetal: Macrosomia, IUD, congenital malformation, **caudal regression syndrome** (sacral agenesis), NTD, anencephaly, VSD, ASD, TOGA, COA, renal agenesis, **single umbilical artery**.
 - **Neonatal:** Hypoglycemia, hypocalcaemia, hypomagnesemia, polycythemia, RDS.
- Insulin is preferred over other oral hypoglycemics as -
 1. Insulin does not cross placenta, so neonatal hypoglycemia is not seen
 2. Pregnancy is a/w increased insulin resistance, so requirement of insulin ↑es.
 3. Some OHA can be teratogenic. (however, **Glyburide** can be used during pregnancy)

Rh - Incompatibility

- When a Rh -ve mother carry a Rh +ve fetus (or husband is Rh +ve) Rh-incompatibility results in.

- Sensitization of maternal blood by Rh antigens (e.g. in amniocentesis, CVS, placental abruption, feto-maternal blood contact) leads to D antigens in maternal blood.
- I/m **Anti-D immunoglobulins** (Rheogram) must be given to mother to prevent hemolysis in present or future fetuses. Doses are
 1. In case of abortion < 20 week --- 50 µg (100 µg in > 20 week abortion)
 2. After amniocentesis or CVS --- 250 µg
 3. Prophylactic to all un sensitized Rh-ve women --- 300 µg (b/n 28 - 32 weeks of gestation)
 4. In case of delivery with Rh-incompatibility --- 300 µg (Give i.m. injection to mother within 72 hr of delivery)
- O.D.D. (Optical Density Difference) and Liley's zone are used to predict outcome. ODD of > 0.1 suggests baby is severely affected by hemolysis.
- *Intrauterine fetal transfusion* with Blood group 'O' Rh -ve packed cells (hct 80%) cross matched with mothers blood should be used to raise hct > 40-50%. Preterm delivery may be needed after 34 weeks.

FETO-MATERNAL HEMORRHAGE (FMH)

- Fetal RBCs in the maternal circulation c/b identified by using acid elution principle or **Kleihauer-Betke counts** (Quantitative test for FMH)
- Apt test is a qualitative test for FMH, which shows presence of fetal hemoglobin in maternal blood. Rarely used now a days.
- K.b. test (The Kleihauer-Betke counts /stain) is a blood test used to measure the amount of fetal hemoglobin transferred from a fetus to a mother's bloodstream.
- Causes of FMH (that may incite RBC antigens to isoimmunization) are :
 1. Early pregnancy loss : Miscarriage, missed abortion, elective abortion, ectopic pregnancy
 2. Prenatal procedures: CVS, amniocentesis, fetal blood sampling.
 3. Others : Idiopathic, trauma, ECV, manual removal of placenta.

FETAL HYDROPS

- Extracellular accumulation of fluid in tissues & serous cavities of fetus .
- If it is without the evidence of immune cause then it is called NIHF (Non-immune HF). There is no e/o circulating antibodies against RBC antigens in NIHF.

- Triad of *Large placenta + skin edema + ascites*
- USG must demonstrate fluid at atleast 2 sites. Criteria: Any 2 of these should be present
 - ↑ skin thickness (> 5mm) on USG : Edema
 - Ascites
 - Pericardial effusion
 - Pleural effusion
- Pathology: severe anemia, hypoproteinemia, heart failure.
- Causes : Non-immune (80-90%) & immune (10-20%)
 - Non-immune causes (NIHF)*
 - Chromosomal: Down's, Turner's, triploidies.
 - Congenital cardiac lesion: Ht block, SVT
 - Cong. : Diaphragmatic hernia, renal anomalies.
 - Hematological: G6-PD deficiency, α-thalassemia
 - Infections: CMV, **parvo virus B19**, rubella, Toxoplasma, syphilis, leptospirosis, Chaga's.
 - Placenta & umbilical cord pathology: Twin to twin transfusion, chorioangioma, uncontrolled DM, severe anemia, idiopathic.

Immune causes (IHF)

Rh incompatibility (more common cause of hydrops)

ABO incompatibility

Remember that ABOi though more common than Rhi but is less severe , so less risk of hydrops in ABOi.

→ Remember the qn. which is asked frequently on NIHP :

NIHF is not seen in --- Answer is Rh incompatibility (as in Rh-incompatibility there is immune hydrops) & Ectopic pregnancy.

IUGR

- Birth weight is below the tenth percentile of the average gestational age.
- Effects on fetus depend upon timing of insult : If the fetus is affected in first trimester symmetrical IUGR results If fetus is affected in 3rd trimester asymmetric IUGR results
- **AC** (abdominal circumference) the single most important (most sensitive & most useful) USG parameter to assess fetal growth in IUGR.

→ 1st trimester ---Teratogenic effects are maximum during 1st trimester (18-56 days)

→ 2nd trimester ---Most rapid growth rate of fetus occurs during 2nd trimester (Insulin has maxm effect)

→ 3rd trimester ---If fetus is affected asymmetric IUGR results

Intrahepatic cholestasis of pregnancy

- Also k/as recurrent jaundice of pregnancy, cholestasis hepatosis, or icterus gravidarum.
- There is pruritus, and icterus in late pregnancy (usually in 3rd trimester).
- Lab/f: S. bilirubin 4-5 mg% (direct), \uparrow ALP. Transaminases (SGOT, SGPT) are normal or mildly elevated.
- Best markers are **bile acids**, which are \uparrow ed 10-100 fold.
- Liver biopsy: Mild cholestasis with bile plugs in hepatocytes (no sign of inflammation/necrosis).
- T/t: Usually self limiting. Ursodeoxycholic acid c/b given to relieve pruritus.

→ In acute viral hepatitis of pregnancy s.transaminases (SGOT/PT) are very high (> 250 IU/L)

Diseases which show improvement in pregnancy

Pregnancy is a state of immunodeficiency so disorders with immunological basis improves in general e.g. sarcoidosis, MG, Grave's disease, SLE, Syphilis, Migraine, Spasmodic dysmenorrhca.

There is no evidence that pregnancy worsen diabetic nephropathy.

Disease transmitted to the fetus from mother

At the time of delivery --- Gonococcus, HSV-2, HBV, HIV

HYPERTENSIVE DISORDER IN PREGNANCY

Preeclampsia

- Definition:** preeclampsia is the development of hypertension ($BP \geq 140/90$) with proteinuria after 20 wk of gestation in a previously normotensive & non proteinuric patient.
- Predisposing factors for PIH**
Primigravida, obesity, Family history of preeclampsia, molar pregnancy, antiphospholipid syndrome, Factor V Leiden mutation, Multiple pregnancy, Renal thyroid, Collagen vascular disease, DM.
- Mild Preeclampsia:**
 $BP \geq 140/90$ but $\leq 160/110$ on 2 occasions at least 6 hr apart & proteinuria 300mg/24 hours but $< 5g/24$ h.

- Severe Preeclampsia: $BP \geq 160/110$ mmHg on 2 occasions 6 hr apart with **proteinuria** $> 5g/24$ hr.

- Hypocalciuria** is a/w preeclampsia.
- Early onset pre-eclampsia (onset of preeclampsia b/w 20 weeks - 32 weeks) is seen in --- APLA, twin gestation.
- Signs of impending eclampsia**
Headache, visual symptoms, epigastric pain, brisk DTRs.
 \downarrow ed urine output due to ARF, pulmonary edema, Intracranial bleeding.
- GFR remains constant.

HELLP Syndrome:

Seen in preeclampsia. It includes

- Hemolysis:** Microangiopathic hemolysis (Bilirubin > 1.2 mg/dl, Burr cells, schistocytes)
- Elevated Liver enzymes :** LDH > 600 IU/L, SGOT > 72 U/L
- Low Platelet count :** < 1 Lakh/mm³
M/m includes immediate termination of pregnancy

M/m of Preeclampsia:

- Prophylaxis:** Low dose aspirin, Calcium, antioxidants, folic acid
- T/t:** α -methyl dopa, labetalol, hydralazine nifedipine (diuretics & ACE inhibitors are avoided d'to teratogenic effects)
 - Mild Preeclampsia or pregnancy < 37 wk --- Conservative m/m
 - Severe preeclampsia > 34 week or pregnancy > 37 wk or unstable patient --- Termination of pregnancy

M/m of Eclampsia:

- It is an obstetric emergency. It can occur anytime antenatal, intrapartum or postpartum (after delivery 24-48 hs)
- DOC for control & prevention of convulsions** is $MgSO_4$. Therapeutic level is 4-7 mEq/L. Magsulph levels should be monitoring using :Urine output, Knee jerk, RR
At the Magsulf levels of
 - ≥ 8 mEq/L \rightarrow Knee jerk is lost,
 - ≥ 10 mEq/L \rightarrow Urine output \downarrow ed < 30 mL/h renal shut down c/b seen
 - > 12 mEq/L \rightarrow Respiratory arrest c/b seen.
- Induction of labour is NOT done instead C-section is preferred.

FETAL BIRTH INJURIES

- **Caput succedaneum:** Diffuse, sometimes ecchymotic, edematous swelling of the soft tissues of the scalp involving the portion presenting during vertex delivery. Seen at the time of birth.
- **Molding of the head** and overriding of the parietal bones are frequently a/w caput succedaneum and become more evident after the caput has receded but disappear during the first weeks of life.
- **Cephalhematoma:** It is a subperiosteal haematoma m/c lies over one parietal bone. It may result from difficult vacuum or forceps extraction. Resolves spontaneously. Can produce/exaggerate neonatal jaundice. There is no discoloration of the overlying scalp, and swelling is usually not visible until several hours after birth. An underlying skull fracture, usually linear can be seen.

PUERPERIUM

- It is the period 6 weeks following delivery.
- Regeneration of endometrium starts by 7th day & occurs from uterine glands.
- Postpartum decidua is shed off known as Lochia. Lochia is seen for 14-21 days.
Lochia rubra (1-4d) --- lochia serosa (5-9d) --- Lochia alba (10-15d)
- Involution of uterus takes 6 wks. (i.e. uterus become a pelvic organ)
Subinvolution of uterus occurs in puerperal sepsis, retained product of conception.
- **Puerperal sepsis**
Commonest route of spread is direct extension
M/c manifestation of sepsis is endometritis
M/c organism involved is streptococcus.

IMP. ASSOCIATIONS

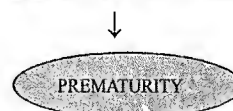
Associations / High Incidence of

Nulliparity	<ul style="list-style-type: none"> ◦ Ca endometrium ◦ Breast Ca ◦ Endometriosis
Primigravida	<ul style="list-style-type: none"> ◦ Hyperemesis gravidarum ◦ PIH
Multipara	<ul style="list-style-type: none"> ◦ PPH, uterine atony ◦ Anemia ◦ Malpresentation (Face, transverse lie) ◦ Choriocarcinoma, Ca Cx

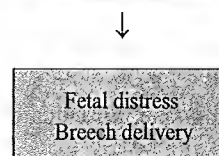
- Multiple sexual partners is a known risk factor for --- Ca cervix, STD's, PID's leading to ectopic pregnancy.
- Adolescent pregnancy has higher risk of --- Anemia, IUGR, preterm labour, high incidence of STDs
- Elderly primi has ↑ risk of --- Molar pregnancy, aneuploidy, infertility, PIH
- Grand multipara has ↑ risk of --- Malpositions, PPH (uterine atony), anemia, labour dystocia

Prematurity

Placenta previa,
Maternal infections,
IUGR,
Polyhydramnios,
Smoking, low SES,
Incompetent cervix



← A/w abnormal presentation



Post maturity

- Anencephaly
- Placental sulfatase deficiency
- Perinatal hypoxia

GESTATIONAL TROPHOBLASTIC DISEASES

H. mole

- Histologically H.mole is c/by hydropic degeneration of the villous stroma (giving it grapes like appearance)
- A/w: PIH, DM, hyperthyroidism
- Histologically H.mole is characterised by hydropic degeneration of the villous stroma (giving it grapes like appearance)
- A/w: PIH, DM, hyperthyroidism.
- A hydatidiform mole conception may be categorized in medical terms as one type of non-induced (natural) "missed abortion"
- High risk GTD if score is >7.

→ Invasive mole is *Chorioadenoma destruens* (Penetrates through muscle layer)

Total and partial mole

Features	Complete/ total mole	Partial mole
• Karyotype	46, XX (46, XY)	Triploid (69, XXY) sometimes tetraploid, (91, XXXY)
• Trophoblastic proliferation	diffuse	focal
• Cellular atypia	+	-
• Serum hCG	↑↑↑	↑
• Risk of choriocarcinoma	2%	less
• Villous edema	++	+, atrophy
• A/w	AB blood group Hyperthyroidism	Vit A deficiency, HTN

T/t of molar pregnancy

- Oxytocin ± suction curettage --- When women wants future pregnancy (curettage is necessary for complete evacuation).
- After evacuation of mole, theca lutein cyst may regress after 3-4 weeks.
- Hysterectomy is TOC in women who has completed family/ passed child bearing age, as there is risk of choriocarcinoma.

CHORIOCARCINOMA

- Most malignant tumour of uterus.
- Persistent or irregular uterine hemorrhage following an abortion, a molar pregnancy or a normal delivery, should always raise the suspicion of chorio Ca.
- Incidence is
 - Maximum after evacuation of H. mole (50% cases/ most commonly) : develops within 2 yrs
 - C~ may appear many years after a spontaneous abortion (in 25%) full term pregnancy (25%) or
 - Extra uterine /ectopic pregnancy (in 5%)
 - Primary C~ arising in the placenta during pregnancy with liver metastasis is extremely rare
- ↑ Risk of development of choriocarcinoma following H. mole is there if

1. Age > 35 yrs
2. Pt with previous 3 or more birth.
3. Initial β- hCG in urine 1,00,000 IU/24 hr.
4. Histologically proven infiltrative mole.
5. Previous H/o molar pregnancy.
6. Women with blood group A or AB with husband group O

Adverse prognostic factors for a gestational trophoblastic tumour

1. β- hCG level > 40,000 IU/ml before therapy
 2. Duration > 4 months
 3. Metastasis to brain or liver
 4. Prior chemotherapy failure
 5. Antecedent term pregnancy
- Majority of growths arise in body of uterus within endometrial cavity. There may be periodic hemorrhage.
 - M/c metastatic sites are lung > brain, liver > g.i.t. Metastasis usually occurs by **blood-stream**.
Can cause multiple **canon - ball metastases in lungs** (on CXR) & may even presents with hemoptysis.
 - USG is 1x of choice. "alveolar snowstorm pattern" is seen.
 - Early metastases may involve lower 1/3 rd of vagina & vulva.
 - Absence of villi in choriocarcinoma differentiates it from invasive mole.
 - T/t
 1. TOC is chemotherapy with Mtx (in patient with liver disease actinomycin-D is used).
 2. Hysterectomy is indicated for :-
 - High risk cases in > 40yr multiparous women --- huge growth in uterus placental site
 - Trophoblastic d/s
 - Hemorrhage d/to uterine perforation
 - Ineffective chemotherapy
- Hysterectomy is preceded & followed by chemo
- Prognosis is excellent with chemotherapy, 100% success rate in low risk group & 90% in high risk gp. Life long follow up may be required.

Indications of chemo in GTD

- Histological e/o choriocarcinoma
- E/o metastases in brain, liver or GIT, or radiological opacities >2cm on CXR. Pulmonary, vulval or vaginal metastases
- Heavy bleeding P/V or GI/intraperitoneal h'age.
- Rising hCG after evacuation/ >20,000 IU/L after 4 wks of evacuation / elevated hCG after 6 month even if falling trend.

GTD's : Patho/Histological features

GTD	Villi	Villous edema	Membrane	Fetal blood vessels
Complete vesicular mole	+	++	+	-nt (avascular villi)
Partial mole	+	-	+	+
Invasive mole	+	-	+	-
Choriocarcinoma	-	-	-nt	-

- TM4SF9 expression in the trophoblasts may relate to their invasiveness and play an important role in the metastasis of trophoblastic tumor. ↑ed in the order of normal villi, hydatidiform mole, invasive hydatidiform mole and chorionic carcinoma

SAMPLE IMP. NEGATIVE POINTS

- PID is NOT common in --- Syphilis
- Rh-isoinmunization risk is NOT ↑ed with --- ↑ maternal age.
- NOT used for surveillance of IUGR --- Laparoscopy
- NOT used in t/t of endometriosis --- Estrogens
- NOT a high risk pregnancy --- History of postmaturity in previous pregnancy.
- NOT a high risk factor for PIH --- Family h/o DM
- NOT a mechanism of IUCD --- Inhibition of ovulation
- Drug NOT used for cervical ripening --- Ergometrine.
- Drug NOT useful in t/t of PPH --- Mifepristone (Misoprostol c/b used)
- Small for date baby does NOT contribute --- PPH
- Normal delivery is NOT possible in --- PMP (Persistent mento-posterior)
(Forceps can NOT be used in --- PMP)
- Intrauterine rubella does NOT cause --- Hutchinson's teeth
- Early clamping of cord is NOT indicated in --- Post maturity.
- NOT a causes of Hyperfibrinogenemia --- Rh incompatibility
- OCP failure is NOT seen with use of --- Beta-blockers
- NOT included in Manning score --- OCT
- NOT a cause of obstructed labour --- CTEV
- Non-immune hydrops is NOT seen in --- Rh or ABO incompatibility
- NOT an unequivocal evidence of heart disease in pregnancy --- Systolic murmur

- Diseases which do NOT show improvement with pregnancy --- carcinoma thyroid, hepatitis, bronchiectasis
- Drug NOT useful for emergency contraception --- DMPA
- NOT a complication of gestational DM --- Hydrocephalus
- Drug NOT preferred to control PPH in a patient of heart d/s --- Methergin
- Drug which can NOT be used to treat PPH in a RHD patient --- Methyl ergotamine
- Manoeuvre NOT to be used in m/m of shoulder dystocia --- Fundal pressure, Mauriceau smellie veit maneuver
- Active m/m of 3rd stage labour does NOT include --- Fundal pressure
- Vacuum extraction should NOT be done in --- Prolonged 3rd stage.
- Expectant m/m of placenta previa does NOT include --- LSCS.
- NOT true for preterm labour --- Prophylactic antibiotics are recommended for intact membranes

CLINICAL VIGNETTES

- A lady comes at 28 weeks of pregnancy with 8 gm% of hemoglobin. Peripheral smear reveals microcytic hypochromic picture. Best m/m option for her would be
[DNB HRH Delhi'08]
 - A. Oral iron tablets
 - B. Injectable iron preparations
 - C. Iron and folic acid tablets
 - D. Blood transfusion
 (Ans.A. Oral iron tablets)
 Oral iron tablets c/b used if we have 7-10 weeks time to build iron stores and Hb is also not too low. Allergic reactions are common after injectable iron, so not preferred. If anemia is severe (Hb is <7) then consider BT.
- A 26 year old female was admitted in delivery room since 12 hours. On PV examination gynaecologist feels "bag of worm" like feel. Most likely presenta" in this case would be
[DNB HRH Delhi'2008]
 - A. Cephalic presentation
 - B. Shoulder presentation
 - C. Cord presentation
 - D. Compound presentation
 (Ans.:C.Cord presentation)
- A primi presents with labour pains & bleeding PV at 36

weeks of gestation. Ultrasound reveals central placenta previa .FHS are normal . Best t/t option for this patient is

[DNB HRH Delhi'08]

- A. Emergency LSCS
- B. Induction of labour
- C. Trial of labour
- D. NVD

(Ans.A:Emergency LSCS)

Diagnostic clues are

- As this is a case of central placenta previa --- NVD is not possible even if the baby is dead
 - Trial of labour/ expectant line of m/m will further aggravate the condition of pt
- Emergency LSCS is required to save the baby

- A 22 year old female with amenorrhoea of 2 months comes with complaints of spotting. O/E cervical os is closed. Urine pregnancy test is positive most likely diagnosis is--

[DNB HRH Delhi'08]

- A. Threatened abortion
- B. Missed abortion
- C. Ectopic pregnancy
- D. Inevitable abortion

(Ans.A:Threatened abortion)

Abortions

Type	Bleeding	Uterine size	Cervical Os
• Threatened	Slight, Painless	= to GA	Closed
• Inevitable	Painful	=/ < than GA	Dilated
• Incomplete	Profuse	< than GA	Dilated
• Missed	Pregnancy symptoms ±	< than GA	Closed

- A 32 year old female with a history of 2 mid-trimester abortions, comes now with 32 weeks of pregnancy and labour pains with Os dilated 2 cm. All are done, except:

[AIPGMEE – 2000]

- A. Immediate circlage
- B. Betamethasone
- C. Antibiotics
- D. Tocolytics

(Ans: Immediate circlage)

Circlage is done in 2nd trimester.

- A woman at 32 weeks of pregnancy, presents with Labour pains. On examination, her cervix is dilated and uterine contractions are felt. The management is:

[AIPGMEE – 2000]

- A. Isoxuprine hydrochloride
- B. Dilatation and Evacuation
- C. Termination of Pregnancy
- D. Wait and Watch

(Ans: Isoxuprine hydrochloride)

Tocolytics should be given to avoid the possible risk of threatened abortion and to buy the 48 hrs time for ANS (dexta) to act.

- A hypertensive primi presents at 34 weeks with pain abdomen, bleeding PV, and loss of fetal movements. O/E, uterus is contracted and uterine tone is increased. FHS are absent. Likely d/g is

[AIPGMEE – 2003]

- A. Placenta previa
- B. Abruptio placentae
- C. Preterm labour
- D. Polyhydramnios

(Ans: B. Abruptio placentae)

APH d/to placental abruption is char/by painful continuous bleeding with tense, tender, rigid (contracted) uterus.

FHS are usually absent

M/m: First priority is resuscitation (correction of shock, BT if needed)

Placental abruption with revealed bleed

(patient presents with bleeding PV)

- Pt in labour → Induction by ARM +/- oxytocin
- Pt not in labour but > 37 weeks → Induction by ARM +/- oxytocin
- Pt not in labour and < 37 weeks
 - If bleeding has stopped or very slight → Expectant/ conservative t/t
 - If bleeding does not stop → Termination of pregnancy by ARM ---oxytocin

Placental abruption with concealed bleed

(pt presents with features of shock but no bleeding PV)

Initially crystalloids (NS/RL) or BT if available → Induction----if failed → LSCS

- A hypertensive primi presents at 38 weeks with painless bleeding PV. O/E, head is engaged and uterus is non tender and relaxed. The next line of M/m is

[AIPGMEE – 2003]

- A. Per speculum examination
- B. Conservative t/t
- C. Termination of pregnancy

D. Ultrasound

(Ans: D. Ultrasound)

Though painless bleeding PV is a feature of placenta previa abruptio should be ruled out as the patient is hypertensive. Ultrasound is best to differentiate b/w AP and PP. After ultrasound M/m plan is

- P/s examination in OT
- If patient presents after 37 weeks (term) → Termination of pregnancy
- If patient presents before 37 weeks (preterm) and
 - If bleeding stops → conservative t/t
 - If bleeding does not stop → Termination of pregnancy by LSCS

Indications for active t/t (not conservative) in APH are
 ---Term / 38 weeks+ pregnancy, patient in labour, patient exsanguinated, bleeding continues, absent FHS, Baby is dead/ congenitally malformed

- A female at 37 weeks of gestation has mild labor pains for 10 hrs and cervix is persistently 1 cm dilated and not effaced. What will be the next appropriate management?

[AIIMS Nov '08]

- A. Sedation and wait
- B. Augment pains with syntocinon
- C. Cessarean section
- D. Amniotomy

(Ans. A. Sedation and wait)

Lady in the above qn is in prolonged labour that too in prolonged latent phase. Labour is considered prolonged when the cervical dilatation rate is less than 1 cm/hr and descent of the presenting part is <1 cm/hr

Prolonged latent phase

Normal duration of latent phase is about 8 hrs in primi and 4 hrs in multi. A latent phase that exceeds 20 hrs in primi and 14 hrs in multi is abnormal.

Expectant management is usually done unless there is any indication for expediting the delivery. Rest and analgesics are usually given.

- A primi presents at 37 weeks of gestation with 10 hours duration of labour. O/e her cervix is 1 cm effaced. How will you manage the case?

[AIPGMEE '11]

- A. Give sedation and watch
- B. Amniotomy
- C. Caesarean section
- D. Oxytocin infusion

(Ans. A. Give sedation and watch)

The patient has just crossed maturity (37 weeks) and she is in latent phase of labour. No risk factors are given. So the best option for her is sedation and watch for spontaneous labour.

- A multigravida female at term is in labor. Her cervix is 2 cm dilated, head per abdomen is 3/5 palpable, and contractions are 2 in 10 minutes lasting 30-35 seconds. After 4 hours, the cervix is 4 cm, cervicography crossed alert line and to its right. What is the comment on progress of labor?

[AIPGMEE '12]

- (A) Arrest of labour
- (B) Protraction of labour
- (C) Normal progress of labour
- (D) CPD

(Ans. A. Arrest of labour)

Arrest of labour is complete cessation of dilatation or descent. For multipara protraction (which precedes arrest) is <1.5 cm dilatation /h.

- A 37 yr old G2P1L1 female with h/o previous LSCS presents to obstetrics department at 37 weeks with BP of 150/100. Her urine albumin is ++. On pelvic examination cervix is found to be soft with 50% effacement. Baby's head is -3, pelvis is adequate and cervical os is closed. What is the most appropriate management step?

[AIIMS Nov '10]

- A. Antihypertensive regime and then induce labour
- B. Wait and watch for 10 days.
- C. Induce labour spontaneously
- D. Do Caesarean section

(Ans. D. Do Caesarean section)

M/m of Pre-eclampsia

Case	Patient profile	M/m in <34 wk	M/m in >37 wk
A	No pre eclamptic features	Antihypertensive and call back after 1 wk	Termination/ wait for spont labour
B	BP is persisting high	Expectant m/m till 34 wk	Termination by LSCS
C	Grave symptoms, no control	Counsel and terminate the pregnancy to save mother	

- A woman comes with obstructed labour and she is grossly dehydrated. Investigations reveal fetal demise. What will be the management?

[AIIMS Nov '08]

- A. Craniotomy
- B. Decapitation
- C. Cessarean section
- D. Forceps extraction

(Ans. A. Craniotomy)

Patient is in obstructed labour with fetal demise. In modern obstetrics destructive procedures are performed rarely. However the only destructive procedure practised today is putting a tube in cranium or debulking /craniotomy which is performed for removal of dead fetus with cephalic presentation in obstructed labour. Forceps extraction is not possible as the patient is already in obstructed labour. Decapitation was being used for transverse lie. Symphysiotomy c/b carried out for breech presentation with IUD.

- Q After a full term normal vaginal delivery the patient went into shock. Most appropriate cause is?

[AIIMS Nov '10]

- A. PPH
- B. Inversion of uterus
- C. Amniotic fluid embolism
- D. Eclampsia

(Ans.A. PPH)

PPH is the m/c cause of hemorrhagic shock after delivery. Inversion of uterus and Amniotic fluid embolism are uncommon. PPH can occur in both NVD and CS. Inversion of uterus and AF embolism must be ruled if a lady goes into shock after an uneventful delivery.

- Q A female has h/o 6 weeks amenorrhoea. USG shows empty uterine cavity. Serum beta hCG titer are 1000 IU. What would be the next step in management?

[AIIMS Nov '08]

- A. Medical management
- B. Repeat hCG after 48 hours
- C. Repeat hCG after 1 week
- D. Serial ultrasound

(Ans. B. Repeat hCG after 48 hours)

Ultrasound at 1000 IU β -HCG levels will not reveal any significant information. So β -HCG should be repeated after 48 hours to see increasing or decreasing trend.

- Increasing trend especially at least 66% rise suggest viable pregnancy
- Decreasing trend or plateauing may be d/to blighted ovum.

uterine US:

- Q If β -hCG is repeated after 48 hours & it shows $\geq 66\%$ rise (doubling of hCG titre) it indicates \rightarrow viable intra uterine pregnancy.
- Q If β -hCG shows $< 66\%$ rise + an empty sac on USG it indicates \rightarrow ectopic.
- Q If there is \downarrow or plateauing of β -hCG titre \rightarrow May be d/ to blighted ovum /Abortion.

- Q 27 year old female with placenta previa with severe bleeding in shock. What is the most likely outcome post delivery

[AIIMS May'10]

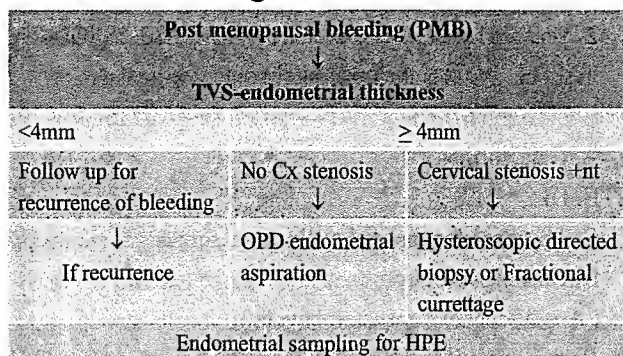
- A. Galactorrhea
 - B. DI
 - C. Absence of menstrual cycle
 - D. Cushing's syndrome
- (Ans.Absence of menstrual cycle)

Postpartum pituitary necrosis has been reported after APH with shock. The condition is k/as Sheehan syndrome and is c/by hypotension with tachycardia, amenorrhoea, lactation failure, breast atrophy. Agalactorrhea is the 1st symptom \rightarrow Lack of return of menstruation (2^o amenorrhoea) \rightarrow Lack of axillary & pubic hair growth.

NOTES

POST MENOPAUSAL BLEEDING (PMB)

Scheme to investigate a case of PMB



- PMB is bleeding PV following established menopause.
- **Aetiology of PMB:**
Senile endometritis and vaginitis, atrophic or hyperplastic endometrium, cervical/ uterine polyp, DUB, TB, Genital malignancies (1/3rd cases are d/to malignancy)
- M/c cause of PMB in India----Indiscriminate use of estrogen for HRT > carcinoma cervix > carcinoma endometrium
- M/c cause PMB ---- Atrophic/ senile endometritis.
- **First line Ix in a case of PMB is-----Hysteroscopic biopsy**
- Risk of Ca endometrium in women with PMB ↑es with age: ~1% at 50 yrs and 25% at 80 yrs of age
- Indiscriminate use of estrogen for HRT leads to endometrial hyperplasia and bleeding. When a woman comes with complaint of PMB it should be f/b curettage. "30-50% cases of PMB are attributed to malignancy of the genital tract."
- In post menopausal women endometrial thickness on TVS should be <4 mm. If it is >4 mm then HPE of the endometrial sample is mandatory.
 - TVS (Trans vaginal sonography) is usually the initial investigation in a patient with PMB
 - Fractional curettage which was first line/ gold standard for PMB, is now replaced by endometrial sampling (endometrial biopsy)
 - Hysteroscopic guided biopsy is now a days gold standard; & is especially useful in setting of focal thickening of the endometrium where blind biopsy may miss the d/g.
 - In case of PMB a definitive diagnosis is made by histology (HPE)
 - Ix of choice in an elderly woman presenting with PMB is endocervical curettage

Scheme to investigate a case of post coital bleed or abnormal pap smear

- If a lady comes with complaints of post menopausal bleed or post coital bleed → Do a **pap smear**
If while taking pap smear or during P/S examination grossly visible growth is found at cervical os → do a **punch biopsy**
- If pap smear shows severe dysplasia → Next step is colposcopic examinaⁿ (visualize ectoCx, endo Cx, TZ)



If colposcopy is abnormal → Next step is **colposcopic directed biopsy & ECC** is mandatory---Treat acc/to biopsy findings

CIN I, II, III---T/t according to stage

Microinvasive/Stage 0---< 3mm → **Conization** / hysterectomy
>3 mm → Radical hysterectomy

Invasive Ca → T/t acc/to stage

- If a 49 yr old lady with 85 kg wt (obese) comes with complaints of abnormal uterine bleed, the physician should first look for → Excess use of estrogen to relieve post menopausal symptom, then endometrial carcinoma.

ENDOMETRIAL BIOPSY

- Done as a OPD procedure by D & C both for diagnostic as well as therapeutic purposes
Diagnostic in : Infertility, DUB, genital TB, PMB
Therapeutic in : DUB, endometrial polyp
- Usually performed in pre-menstrual phase (23-26 days of cycle). It should be done in either clockwise or anti-clockwise direction from fundus to internal os
- Interpretation -
 1. +nce of superficial cells ⇒ Estrogenic phase (proliferative)
 2. +nce of secretory endometrium ⇒ Progesterone phase (cycles has been ovulatory)
 3. Persistence of proliferative⇒ Anovulatory cycle endometrium

- ◉ C/ind : Suspected sepsis or confirmed malignancy to avoid chances of perforation & infection

→ Corkscrew shaped endometrial glands are seen in —late secretory phase.

→ Luteal phase defect can also be diagnosed by E~ (which shows a lag of 2-3 days between calendar and histological dating of specimen).

FERN TEST

- ◉ Ferning is found at the time of ovulation.
- ◉ **Ferning is d/to high NaCl & low protein** present in cervical mucus secreted under **estrogenic activity**.
- ◉ Disappearance of ferning is presumptive evidence of cessation of pre-ovulation phase/appearance of CL activity
- ◉ Pre-ovulation mucous has a great elasticity a phenomena k/as *Spinnbarkeit* / thread test for estrogenic activity.
- ◉ Post- ovulation (secretory phase) mucous is more tenacious/viscous & loses threading, this phenomena is k/as *tack* (It is d/to high progesterone and is a presumptive evidence of ovulation)

LUTEAL PHASE (PROGESTERONE) DEFECT

- ◉ Implies a deficiency in progesterone secretion from CL.
- ◉ Serum progesterone levels on day 8th after ovulation are $< 10 \mu\text{g/mL}$ (value $< 5 \text{ ng/mL}$).
- ◉ Can result from inadequate progesterone receptor induction during follicular phase or d/to deficient secretion of progesterone from ovary.
- ◉ *Endometrial biopsy* is gold standard for d/g.
- ◉ Can cause **recurrent / habitual abortions / infertility**
- ◉ Short life span of CL with a thermal shift of < 12 days
- ◉ R_x : Progesterone either exogenous or endogenous
 - Progesterone suppositories during post ovulatory (luteal) phase can help
 - HCG can \oplus CL to produce endogenous progesterone.
 - Clomiphene citrate
 - HMG (which contain both FSH & LH) \oplus entire ovarian cycle

POST COITAL TEST (Sims/ Huhner's test)

- ◉ Used to evaluate role of **cervical factor** in infertility
- ◉ Performed on *expected date of ovulation (b/n 2 - 16 hr after intercourse)* : immediately before ovulation.
- ◉ A specimen of endocervical mucus is inspected 8-12 hours after intercourse; for clarity, ferning, elasticity, no. & activity of spermatozoa.

- ◉ Couple is advised intercourse close to ovulation time and women is called for test 2 hour later.
- ◉ P~ detects anti-sperm antibodies i.e. **immunological factor** (their presence inhibits movements of spermatozoa).
- ◉ Interpretation
 - +ve test : Any purposeful forward progression of spermatozoa
 - ve test : No sperms/ dead sperms/ < 3 sperms per HPF

→ *Miller-Kurzrok test*

Consist of placing ovulation mucous on a glass slide and studying for penetration by sperms.

→ *Zona-free hamster egg test* is another sperm penetration test.

IDEAL TIMING FOR

◉ Radiological investigations in a young / reproductive age women	1st 10 days of menstrual cycle
◉ Tubal patency test (Hysterosalpingography) /detection of tubal pathology/	5-12 days of menstrual cycle (pre-ovulatory phase)
◉ Fern test	In pre -ovulatory phase
◉ Post coital test	on expected day of ovulation /just before ovula ⁿ
◉ Endometrial Biopsy	23-26 days (pre-menstrual phase)

→ *Dilatation & curettage for D/g of TB from endometrium is carried out in late pre-menstrual phase because tubercles are +nt in superficial layer and shed during menstruation.*

→ *Best test to assess female reproductive cycle — sex steroid hormones*

Conditions which are estrogen dependent	Endometrial hyperplasia is seen in
◉ Endometriosis	◉ PCOD
◉ Endometrial Ca	◉ Granulosa/theca cell tumour
◉ Fibroid	◉ Estrogen t/t
◉ Ca breast	◉ \uparrow ACTH.
◉ Erosion of Cx	

Cells of vagina

- ◉ Maturation index is rarely used now
- ◉ *Vaginal acidity/pH* is estrogen dependent . It is d/to presence of lactic acid & Doderlein bacilli which best grow at pH 4 - 4.5 (highly acidic pH).

Age	pH of Vagina	Predominant cells in vaginal smear
Newborn	5.7	Intermediate cells, transitional epithelium
Infant/ Child	6-8	Parabasal cells
Puberty	4	
Pregnancy	4	Navicular cells
Reproductive life	4.5	Navicular/ Intermediate cells,
Post partum women		Parabasal cells
Early menopause		Intermediate cells,
Late menopause, elderly	>7	Parabasal cells

- Estrogen dominated smears contain-- Clean, discrete, superficial, cornified, polygonal, squamous epithelial cells
- Progesterone dominated smears contain -- Dirty, predominance of intermediate cells (navicular cells)
- Post-menopausal smears contain -- Parabasal and basal cells d/to lack of any hormonal activity

M/c sites for

- Adenocarcinoma (by DES) --- Anterior wall of vagina
- Endometriotic cysts, inclusion cysts --- Posterior wall of vagina
- Hormonal study/ vaginal cytology --- Lateral wall of vagina (upper 1/3rd)
- Pap smear --- Post wall of Cx (Squamo-columnar junction)
- Cervical erosion --- Left lateral wall of Cx (30'clock position)
- Part of hymen which ruptures most commonly/Ist --- Postero-lateral portion
- Bartholin cyst --- At ant. 2/3rd + post. 1/3 rd junction of labium majus (inner side)
- Gartner's cyst --- Antero lateral wall of vagina (10 O'clock position)

- Hymenal tear are m/c in - Posterior > posterolateral portion
- Post-menopausal smears contain -- Parabasal and basal cells d/to lack of any hormonal activity

UTERUS

- M/c congenital anomaly of uterus is *bicornuate unicollis*.
- Septate uterus is the m/c anatomical defect causing recurrent abortions.
- Mucous lining of the uterus is called endometrium. Surface epithelium consists of single layer of ciliated columnar epithelium.

- Endocervix is lined by simple columnar epithelium.
- Ectocervix is lined by stratified squamous epithelium.
- The squamo-columnar junction is situated at the external Os.
- There is NO submucous layer in endometrium of uterus.
- Fallopian tubes are lined by ciliated columnar epithelium.
- Endometrial carcinoma begins from squamocolumnar junction.

- **HYMEN** : M/c configuration of hymen at birth is annular in shape, while the crescentic configuration is most prevalent in children over age 3 years.

- **CERVIX** : Shape of cervical is cylindrical. For women who are nulliparous, or have not given birth, the cervix appears to have a small circular opening (external os) at its center. In parous women, the cervix is bulkier and the external os has a more slit like appearance.

- **Cervix : corpus (body of uterus) ratio** :
Size of body of uterus ↑ as age advances. So Cx: Corpus ratio ↓ as

Age	Ratio
In a female child before puberty (<10yr)	2:1
At puberty	1:2
Reproductive years	1:3
Elderly	1:4

Premature menopause

- Also K/as **premature ovarian failure**
- Cl/f. Secondary amenorrhea for at least 3 months with ↑ FSH, ↑ FSH /LH ratio, and low E₂ level in a woman < 40 yrs of age.
- Autoimmune d/s are reported in 30-60% of patients
- Hot flushes & sweating occur in 75% of patients.

Peri menopausal changes

- Normal LH & normal or ↑ FSH
- Anovulatory cycles of dysfunctional uterine bleeding which is irregular & heavy is d/to excess endogenous estrogen.

(unopposed by progesterone). In obese women additional source is ↑aromatization of androgenic precursor (also seen with liver diseases, thyrotoxicosis)

- Endometrium is at least proliferative & possibly hyperplastic because of unopposed estrogen.

Post menopausal changes

- Vagina:** Thinned and dry epithelium with pale vagina. Basal & parabasal cells are present (superficial cells -nt) ↑glycogen content of cells, Alkaline pH (≥ 7). Senile atrophic vaginitis, leucorrhea, burning, dyspareunia, pruritus
- Hormones:** Estrogen deficiency, ↑gonadotropins (LH & FSH)
- Osteoporosis** (bone loss in axial skeleton in trabecular bone with thinning of cortex) more common in whites.
- T/t:** Estrogen cream, bisphosphonates, SERM.
- HRT** is indicated in menopausal women with co-morbidities. HRT ↓es osteoporosis, colorectal cancer.

PRIMARY AMENORRHEA

D/d of Primary amenorrhea

Condition	Karyotype	Gonads	Breast dvpt	Uterus	Pubic hair
MRKH Syndrome (Mullerian agenesis)	Normal 46 XX	Absent uterus, absent vagina, normal ovary	N	-nt	N
AIS (Testicular feminization ^m)	46 XY	Atrophied vagina	N	-nt	-nt
True/pure gonadal dysgenesis		Normal uterus	No/Under developed		-nt
Turner's	45 XO	Streak gonads	Under developed		↓
Swyer's		Absent ovary	No		
Kallman's	Normal	Delayed puberty + micropenis in males	Absent		

MRKH/Mayer Rokitansky Kuster Hauser Syndrome (Mullerian Agenesis)

- Patient usually presents with normal well developed breasts and pubic hairs but there is absence of vagina and absent uterus.
- Normal hormonal profile**
Normal functional ovaries
Normal secondary sexual characteristics
- Only anatomical abnormalities of reproductive tract are seen --- absent or rudimentary uterus & vagina. Vestigial vagina /vaginal pouch may be seen.
- Secondary sexual characters are normal and there is eugonadotropic (Gn normal) 1^o amenorrhea since ovaries are functional (i.e. Ovaries secrete estrogen, ovulation is normal, and pituitary feedback is normal)
- WNT-4 gene mutation.
- Chromosome 46, XX. Genotype and phenotype female
- A/w renal abnormalities (one kidney may be -nt) & skeletal abnormalities.

Androgen insensitivity syndrome (AIS) (Testicular feminization synd.)

- Genetic male (XY) with phenotypic female
- MIS inhibits uterine development --- Small atrophied vagina but clitoris and breasts are normal
- Testosterone receptors in cytoplasm of target cells are defective



so axillary & pubic hairs -nt.

- Receptor gene is +nt on long arm of X - chromosome (Xq)
- Pubescence occurs normally in patient with testicular feminization, therefore they should not have their gonads removed until after sexual development has occurred (up to 20yr). Breasts are Tanner stage 4.
- DHTA -nt, ↑ level of Gonadotropins (LH & FSH)
- Internal gonads are testes which are intraabdominal/inguinal which mimics inguinal hernia.
- Family history in 30%
- B/L laparoscopic gonadectomy is preferred for removal of testes, as they have a high potential for malignant change, but malignant potential is lower than dysgenetic Y-gonads.

SECONDARY AMENORRHEA

D/d of secondary amenorrhea

Condition	Hormones	Bleeding on hormonal challenge	Other/f
Hypothyroidism	↑ TSH ↑ PRL, Galactorrhea		
Hyperprolactinemia	Normal TSH, ↑ PRL, Galactorrhea		
PCOD (PCOS)	↑ LH, ↓ FSH, ↑ DHEAS	+(P)	Anovulation
Ovarian failure/ Resistant ovary	↑ FSH	+(E+P)	
Hypothalamic/ pituitary failure	↓ FSH, ↓ LH, ↓ Estradiol	+(E+P)	
Asherman's	Normal LH and FSH	-nt	Hysteroscopy +ve

PCOD / Stein Leventhal Syndrome

- Polycystic Ovarian Disease (PCOD) is a condition of androgen excess and **chronic anovulation**.
- M/c cause of hirsutism & virilization in young women.
- A/w : **Obesity, hirsutism, secondary amenorrhoea/ oligomenorrhoea, infertility, endometrial hyperplasia/ carcinoma**
- Patho: B/L enlarged ovaries with subcortical cysts (thecal cell hypertrophy and multiple follicular cysts give rise to "necklace appearance")
- Lab/f:
 - ↓ level of FSH & progesterone (which may be absent)
 - FSH/LH ratio is reversed it is 1:3 in PCOS
 - No ovulation → no CL → no progesterone
 - ↑ LH, Estrogen, inhibin (↑ **androgens** in 50%, ↑ androstenedione, ↑ DHEAS, ↑ testosterone), abnormal GTT d/to **insulin resistance** or hyperinsulinism
- ↑ Risk of : Ca ovary, Ca endometrium
- R_x : **Clomiphene** is DOC. Other useful drugs are : GnRH, FSH, HMG.

→ Urinary 17-Ketosteroid excretion is normal in PCOD (As adrenal is not implicated)

→ D/d : Adrenogenital syndrome in which 17- ketosteroid and estrogen excretion in urine is increased

D/d of hirsutism, amenorrhea and obesity in a female

	Karyotype	Hormones	Other/F
PCOS (Stein Leventhal)	XX < 20 yrs.	↓ FSH ↑ LH, ↑ E	Triad of obesity +hirsutism + oligomenorrhea
Cushing's syndrome	F > M XX, 20-40 yrs	↑ urinary cortisol	hirsutism, amenorrhea, central obesity
Adrenogenital synd. (CAH)	XY	↓ LH	Premature virilization, small testis

Asherman Syndrome (Fritsch syndrome)

- Results from **vigorous curettage (D&C)**, hysteroscopic procedures, post abortal/puerperal infections, uterine packing for PPH etc. leading to adhesions & synechial formation in uterine cavity.
- M/c seen after curettage for MTP & after abortions. A D&C is the m/c cause of uterine synechiae & Asherman syndrome.
- C/f Amenorrhea & infertility.
- D/g is confirmed by hysterosalpingography or direct hysteroscopic visualization.
- C/c – risk of placenta accreta in future.
- T/t is hysteroscopic **synechiolysis** f/b post procedure **insertion of Cu-T** along with oral estrogens are advised to prevent post-op adhesions.

DUB

The etiology of DUB (i.e. abnormal uterine bleeding) is purely hormonal and that the hypertrophy and hyperplasia of the endometrium are induced by a high titre of estrogen in the blood. (Resulting in proliferative endometrium)

→ Cystic glandular hyperplasia is seen in metropathia hemorrhagica.

→ In 80% cases DUB is due to anovulation.

→ Estrogenic phase of menstrual cycle is characterized by proliferative endometrium and progesterone phase by secretory endometrium.

Mittelschmerz

- Mittelschmerz is the pelvic pain that some women experience during ovulation.
- Ovulation generally occurs about midway between menstrual cycles. Mittelschmerz is a German word for "ovulation pain" or "midcycle pain".

SOME DEFINITION

- Precocious puberty in female (onset of secondary sexual characteristics) < 8 yr, in male puberty < 9 yr.
- Precocious menstruation in female if menses start < 10yr.
- Delayed puberty in female >14 yr-16yr, in male > 17yr
Delayed menstruation if menarche fail to occur by 17 yr.
- Elderly primi --- a primi of 30 + yr
- Grand multipara --- a pregnant mother with past H/o ≥ 4 viable births.

Uses of Estrogens Vs progestogens

Progestogens	Estrogens
<ul style="list-style-type: none"> • To suppress pituitary Gn (POP \rightarrow birth controlling pills) • Prophylactic in PCOD (to prevent hyperplasia) • Palliative in EndoM & breast Ca. • Rx of Endometriosis, Threatened / habitual abortion • In conjunction with estrogen to induce progestational effect on estrogen primed endometrium (diagnostic test for evaluation of amenorrhea) 	<ul style="list-style-type: none"> • Rational use in post-menopausal women (HRT) • T/t of gonadal failure, control of fertility • T/t of Ca Breast • T/t of DUB
Metabolic effects	
<ul style="list-style-type: none"> • \downarrow HDL (esp 19- nor testosterone derivatives) • \downarrow T-cell function, \downarrow CMI • Natriuretic action (which also stimulates aldosterone) 	<ul style="list-style-type: none"> • \uparrow HDL & TG-Level • \uparrow Level of proteins secreted by liver (CBG - cortisol, TeBG / Testosterone, TBG - Thyroxine)
<ul style="list-style-type: none"> • C/ Ind. 	<ul style="list-style-type: none"> • C/Ind Pregnancy (may result in vaginal adenosis)

\rightarrow Sensitivity of uterine musculature is enhanced by estrogen & inhibited by progesterone.

DRUGS AND HORMONAL PREPERATION

Drugs used for Ovulation

Induction	Inhibition
<ul style="list-style-type: none"> • Clomiphene citrate (\oplus FSH, LH release) • GnRH (stimulate pituitary FSH & LH, folliculogenesis), Gn (Commonly used : HMG, urofollitropin, hCG) • LHRH (Gonadorelin) • Bromocriptine (for hyperprolactinemia) • Letrozole (superior to clomiphene) • Prednisolone (for women with anovulation and \uparrow androstenedione) 	<ul style="list-style-type: none"> • OCPs • Centchroman

\rightarrow All above mentioned drugs of ovulation induction are useful in T/t of infertility

\rightarrow Clomiphene citrate & bromocriptine are most widely used.

\rightarrow Estrogen & progestin replacement are also useful for t/t of infertility. But combined oral pills are not preferred for those patient who desire to conceive

Drugs useful in t/t of female hirsutism

Female hirsutism is seen in PCOD, masculinizing ovarian cancers etc

- Spironolactone
- Finestride
- Flutamide

GnRH (Buserelin, Factrel, Goserelin) analogue are useful in

1. Precocious puberty,
2. Menstrual abnormality,
3. DUB, infertility caused by PCOD & endometriosis,
4. Cryptorchidism in males,
5. To shrink size of fibroid pre-operatively,
6. Induction of ovulation in anovulation

Danazol is useful in

1. Endometriosis
2. Fibroids
3. DUB
4. FCD (Fibrocystic d/s) of breast

5. In some cases of menorrhagia as last resort.
6. Last resort in some cases of precocious puberty.

Danazol should not be given in hirsutism.

INFECTIONS

PID

- **Ascending infection** is common in gonorrhoea. Mucus membrane is involved first. The inflammatory exudate is discharged into lumen which distends mainly at ampullary end. Ulceration of mucosa leads to adhesions, tubal blockage and narrowing of lumen.
- In acute PID **m/c** complaint is abdominal pain.
- Classic triad of **cl/f** : **Pelvic pain + Cervix motion tenderness + Adenexal tenderness**
- In chronic PID constant low abdominal pain which gets worse before menses. O/e '**Frozen pelvis**' is found.
- Virgin girl with PID is tubercular in nature.
- **M/c** cause of PID is STDs. Gonococcal and Chlamydial infections are common.
- IUCD use ↑ risk for PID while barrier method prevents STD and PIDs.
- Higher rate of bacterial vaginosis is found in woman with PID.

T.B. of Genital Tract

- **M/c** site of genital TB is --- **Fallopian tubes**.
- Age group affected is 20-30 years.
- **M/c** mode of spread is hematogenous
TB of FT/ Genital TB - Hematogenous spread (While in TB of endometrium --- Retrograde Spread)
- Uterus is affected by the infection descending from the tube (retrograde).
- **Infertility** is **m/c** presentation. Other symptoms/signs are: Amenorrhea, dysmenorrhea, dyspareunia, menorrhagia etc.
- **Tobacco pouch** appearance and frozen pelvis occurs in ex-salpingitis.
- **D/g** is made by HSG (hysterosalpingiography) in late premenstrual phase (contraindicated in active d/s),
 - Rigid non peristaltic "lead pipe appearance" of tube/ Golf club appearance
 - Beading and variation in filling density, Maltese cross/ rossette type appearances
 - Cornual block, calcification of tube

- **Tobacco-pouch** appearance & dilated distal end of the tubes.

- Hysteroscopy reveals pale endometrial cavity with multiple adhesions obliterating cavity.
- Laparoscopic biopsy taken from tubes or other affected area.
- **T/t**
 - ATT (first line T/t)
 - Surgery

Indications are progression of d/s, persistence of symptoms/ active lesion/mass/fistula despite chemo Tuboplasty is contraindicated, as it may cause reactivation of T.B.

- **P/g:** Pregnancy rate is only 10% of which only 2% women have live born child.

TB of Lower genital tract (Vulvovaginal TB)

- Rare, constitute 1-2% of genital TB
- Usually secondary to extension from endometrium or cervix. Sometimes primary d/to transmission from infected partner
- Presents as hypertrophic lesion or a **non-healing ulcer of vulva or vagina**, mimicking malignancy.

Syndromic management of vaginal discharge

- Essential components of syndromic m/m are --- D/g and t/t based on syndromes, education on risk reduction, condom provision, counselling, partner notification, follow up.
- Vaginal discharge is caused by either vaginitis or d/to cervicitis

VAGINITIS

- D/to Trichomonas vaginalis, candidiasis, bacterial vaginosis:
- T/t of Trichomonas vaginalis and bacterial vaginosis: Metronidazole 2 g orally single dose
- T/t of Candidiasis: Fluconazole 150mg orally single dose + Clotrimazole pessary 100 mg intravaginally x 6 days

CERVICITIS

- Commonly d/to Neisseria gonorrhoeae or Chlamydia trachomatis. Other organisms causing cervicitis are : staph, strepto, , E.coli etc.
- Recommended t/t is tab azithromycin 2 gm orally under supervision.

Erosion of Cx

- Common & often recurrent in cervicitis.

- Estrogen is mainly responsible for erosion of Cx.
- Apart from birth it may occur before puberty or after menopause.
- Ectopic squamous grows downward k/as epidermalization which looks like epidermoid carcinoma but it is neither malignant nor premalignant.

■ Inflammation of Cx

May lead to formation of Nabothian follicle.

■ Gartner Cyst

Cyst arising in duct of Gartner (duct of epoophoron)

■ Bartholin Cyst

- Chronic cyst d/to blockade of Bartholin's ducts either d/to inflammation or accumulation of secretions of Bartholin's glands.
- Usually an w/L swelling which bulges across vaginal introitus and produces discomfort, dyspareunia.
- M/c site : On inner side at junction of ant.2/3rd and posterior 1/3rd of labium majus
- T/t: Marsupialization.

■ Bartholin abscess

- D/to gonococcus.

■ Vulval hematoma

- D/to improper suturing during episiotomy.

■ Pyometra

- M/c cause is carcinoma endometrium. Other causes are--atresia of vagina, senile endometritis, tubercular endometritis, radiotherapy.

■ Hematocalpos

- Vagina fills with menstrual blood (usually d/to an imperforate hymen).

■ Hematometra

- Collection/retention of blood in uterus. Can present as acute abdomen. Cervical stenosis, cervical fibroid can lead to hematometra.

Gynaecological STDs

- *Bacterial vaginosis (BV)* is caused by mixed flora which includes *Gardnerella vaginalis*, *Mycoplasma hominis*, anaerobic bacteria like *Mobiluncus*, *Prevotella* / *Bacteroides/Peptostreptococi*.

- **Clue cells** are classically seen in *Gardnerella vaginalis* but c/b seen in *Trichomoniasis* also. Clue cells are stained by NaCl. Nugent's criteria to quantify or grade bacteria in BV.
- *The Whiff test* may be positive in up to 70% of BV patients. This test is performed by placing a drop of 10% KOH on slide.
- **Syndromic management of STDs (or STIs)** is applicable to sexually transmitted infections -
Genital herpes HSV, Syphilis, Chancroid, HIV

Feature	Trichomoniasis	Vulvovaginal Candidiasis	Bacterial vaginosis
Organism	Trichomonas vaginalis	Candida albicans	G. vaginalis, H. Vaginalis
↑ risk / A/w	Poor hygiene	DM, Pregnancy, OCP, steroids, condom use	↓ lactobacilli from flora
pH	≥ 4.5	4 - 4.5	≥ 4.5
Discharge	Profuse, thin, creamy or greenish yellow, frothy +/-	Profuse, curdy white	White, milky, non viscous, fishy /seminal odour discharge, frothy (bubbles)
Saline wet mount	Motile protozoa		Clue cells
KOH test	Whiff test +/-	Pseudohyphae+	Whiff test+
Pruritus/ Vulvar irritation	+	++	-
Sp/f	Strawberry Cx / flea bitten Cx on colposcopy, Dyspareunia	White plaques or patches,	Clue cells stained by NaCl like Whiff test
T/t	Metronidazole for both partners	Antifungals	Metronidazole

- Vulvectomy can be done in chancroid & warts.

UROGENITAL FISTULAE

- VVF (Vesico-Vovaginal fistula) are the m/c genital fistulae.
- Continence & incontinence both are seen in VVF
- Pubourethral ligament injury causes long term stress incontinence.
- 3 Gauze swab test / methylene blue test is investigation of choice for D/d.
- M/c cause of rectovaginal fistula : Complete perineal tear (3^o) which is usually repaired within 24hr otherwise after 3 mth (if presenting late)
- The m/c type in our country is vesicovaginal fistula at the bladder neck region following difficult childbirth (obstructed labour). In India obstetric fistulas are more common > than gynaec.

Fistulae	Vesicovaginal (VVF)	Ureterovaginal (UVF)	Vesicouterine (VUF)
M/c site	Bladder neck B/w bladder & upper 1/3rd vagina (ant.vaginal wall)	Distal to uterine artery in cardinal ligament	
M/c cause	<u>Obstructed labour</u> (Pressure necrosis)	Injury to ureter (7-10 day after gynaec operation/ Wertheim's hysterectomy) continuous flow of urine	Caesarean section
Symptoms	Continuous flow of urine/true incontinence		Continence is retained, <u>Cyclical Hematuria</u>
Repaired after	3 month. Chasner's technique	6 mths	

- M/c urinary fistula --- Vesicovaginal
- M/c cause of VVF --- Obstructed labour
- M/c cause of UVF --- Injury to ureter after gynecological operations esp. Wertheim's operation.
- M/c cause of VUF --- Caesarean section
- M/c cause of RVF --- Complete perineal tear

Stress urinary incontinence (SUI) :

- Pubourethral ligament injury causes long term stress incontinence.
- Medical t/t with Duloxetine.
- Procedure with highest success rate in SUI are :
Burch's calpo-suspension (89%) > Kelly's repair (50-60%)

PROLAPSE

Supports of uterus

Primary support

- Muscular or active support
- Pelvic diaphragm (levator ani), perineal body, urogenital diaphragm (deep transverse perineal)
- Fibromuscular or Mechanical supports
- Uterine axis, pubocervical ligament, transverse cervical ligament, uterosacral ligament, round ligament of uterus

Secondary (false) supports

- Broad ligament,
- Uterovesical fold of peritoneum, rectovaginal folds of peritoneum

Genital Prolapse

- M/c cause of genital prolapse is torn perineal body.
- M/c type of genital prolapse is cystocele.
- Stress incontinence is seen in vaginal prolapse.
- Risk factors a/w prolapse: Menopause, birth injury, chronically ↑ed intra abdominal pressure - constipation, obesity, pelvic floor trauma.

M/m of prolapse

Non-operative + prevention of prolapse

- Abdominal and perineal exercise
- Intrapartum and antenatal care

Pessary t/t

1. Used in early pregnancy i.e. first trimester
2. Periparturient women with severe degree of prolapse
3. Unfit for surgery, high risk for surgery

For vault prolapse

Right transvaginal sacrospinous colpopexy (in obese and elderly, not fit for surgery)
Transabdominal sacral colpopexy using Mersilene mesh extraperitoneally.

- Shirodkar stitch are applied in incompetent os around 14 wk (maximum upto 3 months).

Surgical options

Patient profile	Type of prolapse	Surgical T/t of choice
1. Young nulliparous	2° or 3°	Abdominal sling (Purandre, shirodkar's)
2. Multipara presenting in early pregnancy	-	Ring pessary upto 2nd trimester (18-20 wk)
3. Multipara presenting in late pregnancy	-	Ring pessary → delivery → Fothergill repair
4. Multipara <40 desiring child birth	2° or 3°	Fothergill/ Manchester repair
5. Multipara >40, family completed	-	Ward Mayo's vaginal hysterectomy (with ant. Colporrhaphy + posterior colpoperineorrhaphy) with pelvic floor repair
6. Enterocoele	-	Moscowwitz repair

Cervical incompetence

- Circage operation (tracheloplasty), also k/as a cervical stitch, is used for the t/t of cervical incompetence
- McDonald cerclage is m/c & done around 12-14 wk.
- Shirodkar cerclage is applied less commonly.

MYOMAS (FIBROIDS)

- Myomas or fibroids are m/c pelvic tumours. M/c age group affected is 35-45 years
- Conditions or d/s a/w myomas are :
Endometrial hyperplasia, endometriosis, follicular cyst of ovary, endometrial cancer.
- Progesterone inhibits growth of myomas (whereas estrogen stimulates it). OCP should not be prescribed to a women who has diagnosed to have fibroid because fibroid may grow in size under estrogenic influence.

- M/c histological types -- Intramural > submucous > subserous myoma
- Malignant change is m/c in -- Submucous & intramural fibroid
- Cyclical retention of urine in -- Cervical myomas
- Torsion is common in -- Large pedunculated subserous
- Inversion of uterus, metrorrhagia, recurrent pregnancy losses are common in -- Submucous fibroid

- M/c symptom of fibroid is menorrhagia not amenorrhea. Menorrhagia is seen in submucous + intramural myomas.
- If sub-mucous myomas are near cornu chances of infertility are more.
- There are three types of Myomas

Myoma type	Characteristics	Complications
S/M Sub-mucous		<ul style="list-style-type: none"> ◦ Abortions. ◦ Meno-/Metro- rrhagia (d/to ulceration/ <u>heavy menstrual bleeding & anemia</u>) ◦ Inflammatory changes ◦ Malignant changes ++
I/M Intra mural	M/c histological type	<ul style="list-style-type: none"> ◦ May cause <ul style="list-style-type: none"> - 1st trimester bleeding - Abruptio placentae - Obstructed labour (If it is in lower ex segment) ◦ Preterm labour
S/S Subserous		<ul style="list-style-type: none"> ◦ Pressure effects <ul style="list-style-type: none"> 1. On rectum → Constipation 2. Ureter → hydronephrosis ◦ Pedunculated & serous do not cause anemia (meno/metrorrhagia less) but torsion may occur (<u>wandering fibroid</u>) ◦ Fibrous/calcific/hyaline changes are common ◦ Pseudo Meigs syndrome

- C/c
 - Torsion
 - Hemorrhage
 - Infection
 - Ascites (Pseudo Meigs syndrome)
 - Malignant change
- Degeneration
 - Atrophy
 - Red degeneration
 - Hyaline /fatty/myxomatous degeneration
 - Cystic degeneration

- Effect of pregnancy on fibroid
 - Red degeneration
 - Infection
 - Torsion
 - ↑ed growth of tumour
- Effect of fibroid on pregnancy
 - Infertility
 - Abortion, placental abruption
 - Malposition of fetus
 - Obstructed labour

- M/m
Fibroid in pregnancy is managed conservatively
Medical management :Indications
 - To treat anemia & improve Hb
 - To reduce size of myoma to fascilitate surgery

- To preserve fertility
 - To avoid surgery in unwilling pt and near menopausal women
1. Drugs to reduce Size ---
Danazol, **Mifepristone**, GnRH analogues
 2. Drugs to decrease blood loss ---
Mifepristone, Danazol, Antifibrinolytics, GnRH agonist, Progesterone.

Surgical Management: Indications are

- Menorrhagia, Pressure symptom
 - Infertility or recurrent abortion
 - Malignancy
 - Rapidly growing fibroid
 - Fibroid > 12-14 wk of pregnancy
1. Myomectomy
 2. Hysterectomy—Uncontrolled bleeding during myomectomy, women >40yr, multiparous women, malignancy

Red degeneration of fibroid

- Develops most often in **second trimester** of pregnancy
- Myoma becomes tense & tender & it causes severe abdominal pain
- Aseptic condition
- Lab/F : raised ESR, leucocytosis
- Patient is treated conservatively with bed rest & analgesics.

INFERTILITY

- If a couple (<27 years) fails to achieve pregnancy after one year of unprotected & regular sexual intercourse. (6 months in c/o > 27 yr old couples)
- **Clomiphene Citrate:** It is the **agent of choice for ovulation induction** in women with oligomenorrhea or amenorrhea not having sufficient ovarian function to maintain estrogen levels. Letrozole (aromatase inhibitor) is another drug.
- **Ovarian hyperstimulation syndrome:**
 - Produced by ovulation induction agents like clomiphene citrate, FSH/ LH, GnRH etc.
 - There is increase in vascular permeability leading to third space fluid accumulation manifested by ascites and hydrothorax.
- M/c cause of infertility → Female factor in 58% cases (menstrual abnormalities i.e. amenorrhea and ovulatory dysfunction accounts for 48%).

- M/c cause of female sterility → Salpingitis.
- M/c cause of impotence → Psychogenic
- **Assisted reproductive techniques:**
 - IVF-ET:** In vitro fertilization and embryo transfer.
 - DIPI:** Direct intra-peritoneal insemination
 - GIFT:** Gamete intra-fallopian transfer
 - ZIFT:** Zygote intra-fallopian transfer
 - ICSI:** Intracytoplasmic sperm injection
- **Male factor infertility:**
 - Sperm count < 13.5 million/ml
 - < 32% progressive motility
 - < 9 normal morphology
 - Infertility ↑es with no of abn parameter. With 1 factor 2-3times, 2f 5-7 & with 3f 16times. Options are IUI, IVF, ICSI

T/t of choice / DOC in

• Asherman syndrome	Hysteroscopic dilatation (D + C with IUCD insertion)
• Stein - Leventhal syndrome	Clomiphene citrate
• Post pill amenorrhea	Clomiphene citrate
• Ovulation induction in-patient who bleed in response to progestin challenge	Clomiphene citrate
• For ovulation induction in patient with hypoenestrogenemia, hypothalamic amenorrhea (Progestin challenge -ve)	HMG [Human menopausal gonadotropin]
• Ovulation induction in-patient with primary ovarian failure	Steroid / IVF with donor oocyte

Endometriosis Vs Adenomyosis

- Scar endometriosis can occur following LSCS, hysterectomy, episiotomy.
- Pregnancy causes atrophy of endometrioma d/to high progesterone levels.

	Endometriosis	Adenomyosis
e Common	Young nullipara (30-40 yrs)	Multipara (40 +)
e Risk factor	Poly - menorrhagia	Multipara (40 +)
e Patho	Cystic spaces are formed k/as chocolate cyst of ovary or endometrioma <i>Pseudoxanthoma cells</i> are seen	
e M/c site	Ovaries (m/c site) > uterosacral ligament > pouch of Douglas > fallopian tubes > recto-sigmoid <i>E~ does not occur in vagina, vulva.</i>	Uterus
e Triad of	<i>Infertility + dysmenorrhea (m/c symptom) + dyspareunia</i>	Menorrhagia is the m/c symptom.
e C/F	Yellowish brown fluid in cul-de sac and Blackish puckered spots in post. fornix.	Menorrhagia with progressively ↑ing dysmenorrhea Uterus enlarged but <14 wk size, may be tender.
e Hormonal influence	Estrogen dependent	-
e Dx	Laparoscopy	Laparoscopy
e Rx	Cyclic OCP's. (for mild E~ in young pt)	Hysteroscopic curratage or Local excision in young women, TAH in elderly

GYANAEC CANCERS

Ovarian tumours

- o Ovarian cancers are m/c cause of death among all gynecological malignancies
- o M/c ovarian tumour – epithelial carcinomas (comprise 60% of all ovarian tumours & > 90% are malignant)
- o Ovarian cystadenocarcinoma is m/c malignant tumour of ovary (33 - 50% of epithelial cancers).
Serosus cystadenoma is overall m/c tumour of ovary

- o M/c ovarian tumour in < 20 year of age group --- germ cell tumour.
- o M/c ovarian tumour overall → serous cystadenoma.
- o M/c benign ovarian tumour → serous cystadenoma.
- o M/c malignant ovarian tumour → serous cystadeno Ca.
- o M/c ovarian GCT → Dysgerminoma.
- o M/c benign ovarian GCT → Teratoma
- o M/c ovarian tumour which present as large abdomen/ acute abdomen → Mucinous cyst adenoma

Classification

	Example	Characteristic finding/ Remark
Epithelial tumours	Serosus (50%)	Psammoma bodies
	Mucinous (25%)	
	Endometroid (15%)	
	Clear cell (5%)/ Mesonephroid Ca	Hobnail cells
	Brenner's	Walthard cell nest
Germ cell tumours (mesenchymomas)	Mature Teratoma	Rokitansky's protuberance
	Dysgerminoma	u/L, b/L 15% Radiosensitive tumour a/w Turner's
	Yolk sac tumour/ Endodermal sinus tumour	100% u/L, Schiller Duval bodies, Secrete AFP, α_1 AT
	Choriocarcinoma	
	Embryonal	
	Hilus cell tumour	Rare virilising tumour a/w Reinke's crystals
Stromal tumours	Granulosa cell	Call Exner bodies, Secrete estrogen
	Theca	
	Sertoli	
	Leydig	

Tumour Markers for Ovarian Tumours

- o CA 125 is a glycoprotein useful in post menopausal women. Levels > 35 units /mL are suggestive of residual tumour and need for chemotherapy.

Marker	Chemically	Level ↑ in	Also ↑ in
CA 125	GP	Malignant epithelial Ca	
CEA		GCT (mucinous ovarian tumour)	Endometriosis, abdominal TB
AFP	Onco fetal antigen	GCT Endodermal sinus (Yolk sac) tumour	
β-hCG	GP	Choriocarcinoma	
Inhibin		Granulosa cell tumour	
Placental ALP		Dysgerminoma	

- In endodermal sinus tumour → AFP, α₁ AT
- In endometrioid tumour → CA 125
- Dysgerminoma → neutral secretes placental ALP and LDH
- In seminoma → β-hCG (in 10%) only
- In non seminoma → β-hCG and AFP

Dysgerminoma

- Encapsulated tumour which is 85-90% u/L (only germ cell tumour which is bilateral)
- It is neutral (not secrete AFP) but secrete placental ALP & LDH
- Female counter part of seminoma
- A/w Turner's syndrome
- Highly radiosensitive

Granulosa cell tumour

- It is the m/c estrogen secreting ovarian tumor (sex cord stromal tumor)
- Call Exner bodies are seen
- Hyperestronism → endometrial hyperplasia → ↑risk of Ca-endometrium
- Metastasis are interesting because opposite ovary 1st becomes involved then lumbar region and then mesentery.

Ovarian fibroma

- It is a benign sex cord stromal tumor.
- Meig's syndrome is a/w it.
(Ascites + Rt. pleural effusion +nt)

Dermoid cyst

- M/c germ cell tumour.
- M/c benign ovarian tumor, affecting women of reproductive age group.
- M/c site of teratoma in the body.
- Usually bilateral. M/c tumour in pregnancy
- Malignant change can occur (SqCC in adults and endodermal sinus tumour in children).
- Unilocular cyst with smooth surface, contains sebaceous material, hair, teeth, bone, cartilage etc.,
- If bone & teeth seen in X-ray, it is pathognomic of teratoma
- Rokitansky body/protuberance is seen.

Krukenberg's tumour

Metastatic carcinoma from g.i.t. (most commonly Ca-Stomach) may cause secondary involvement of ovary k/as K~. Characteristics are –

- B/L, smooth surfaces, intact capsule freely movable in pelvis.
- Tumour retains the shape of ovary.
- Histology- *signet ring cells*, solid waxy consistency.
- Primary most often arise in stomach (70%) >large bowel (15%) >breast (6%)
- Arise by retrograde lymphatic spread.
- Highly malignant

- M/c cause of Krukenberg tumor is metastasis from a primary gastric adenocarcinoma (*signet ring type cells are seen & bilateral ovarian metastases*).
- M/c ovarian tumor a/w pseudomyxoma peritonei — Mucinous cystadenocarcinoma
- M/c ovarian tumor a/w hyperthyroidism --- Germ cell tumour with struma ovarii
(*struma ovarii is a teratoma with thyroid tissue*).
- Ovarian tumours with calcification
Cystic teratoma / dermoid cyst (bone ± teeth), Gonadoblastoma, Fibroma
- Torsion of ovarian cyst is m/c complication and is seen in teratoma / dermoid cyst most commonly.
- Ovarian tumour most prone to undergo torsion during pregnancy is --- dermoid cyst.

Parovarian cysts

Extra peritoneal cysts lying in broad ligament adjacent to ovary, below the fallopian tube. Arise from mesonephric duct. Contains clear fluid, its wall is smooth, thin, transparent, and unilocular At laparotomy it is identified as broad ligament cyst

Can undergo torsion. Displaces uterus to opp. side. Rx surgical removal as it attains large size.

- Fallopian tube cancer presents as watery or blood stained discharge per vaginum, pelvic mass and pelvic pain.
- Cervical cancer patients presents as post coital bleeding, menometrorrhagia, continuous bleeding, leukorrhea.
- Ovarian cancer presents as abdominal discomfort, pain and mass.
- Endometrial cancer presents as abnormal vaginal discharge (90%). Postmenopausal bleeding (80%) Leukorrhea (10%)
- T.B. of GUT patients presents with infertility (35-60%), menorrhagia (40%), secondary amenorrhea (10%)

T/t of CIN & Cancer Cx

Cancer	Stage	Treatment
Dysplasia & CIN	Mild, CIN-I	Treat inflammation & follow up 3-6 monthly by pap smear.
	CIN-II, CIN-III	Eradication of entire transformation zone - Conization - Laser/cryo [LLETZ] - Excision & cone biopsy
	CIS (0)	Same as in CIN-III
Ca Cervix	Stage-I IA ₁	1. Cone excision (with -ve margins) 2. Hysterectomy for old
	Stage-II IA ₂ IB, IIA	Radical hysterectomy with B/L pelvic LN dissection (Wertheim's, Mitra's) If LN's are +ve: External radiotherapy
	IIB - IV IIB, III, IV	Radiotherapy

- 40 yr old woman with Pap smear showing CIN-III, best t/t is → Colposcopy + LEEP
- G₃P₂A₀ woman with carcinoma in situ of cervix, best t/t is → Cone biopsy + abdominal hysterectomy
- T/t for CIN + endo-cervical canal involvement, TZ is not completely seen → Cone excision or conization (or there is discrepancy in findings of cytology, colposcopy, and biopsy)
- Best t/t for bulky barrel shaped endo-cervical tumour → Pre-op RT → surgery
- Best t/t for unresectable, advanced and recurrent cervical cancer → Preop chemotherapy → surgery/ RT

Points Of Special Mention

- Treatment of CIN grade-III in 40 year old female (family completed, a/w other gynaec problem) --- Hysterectomy + ovarian removal
- If 47yr old peri menopausal women is having irregular menstrual cycle with heavy menses i.e. menorrhagia --- First to do endometrial biopsy and give only cyclic progestin replacement. Estrogen can cause endometrial hyperplasia (will pronounce more blood loss.)
-- If showing estrogen deficiency symptom but uterus is -nt (& myomectomy done)
give estrogen replacement along with progestin to oppose estrogen & to prevent endometrial hyperplasia. Monitor with USG.
- If uterus -nt (hysterectomy done) = Only estrogen replacement required

SOME IMPORTANT NEGATIVE POINTS

- Morbid adhesions of uterus are NOT seen in --- Bicornuate uterus
- Intramural leiomyomas are NOT a cause of --- APH
- Drug NOT useful in t/t of hirsutism in female --- Oxynandralone
- Hematocolpos is NOT caused by --- Cervical atresia [it may cause Hematometra]
- NOT used in endometriosis --- Tamoxifen (because it causes endometrial proliferation)
- Drug NOT used in treatment of hot flushes --- Tamoxifen
- Arias stella reaction is NOT seen in --- Salpingitis isthmica nodosa
- Mullerian Wolffian duct both are NOT seen in --- FSH receptor mutation.
- AFP is NOT ↑ in --- Pure choriocarcinoma, dysgerminoma
- NOT a/w PCOS --- Osteoporosis
- Menstrual cycle progression can NOT be assessed by --- Estrous profile.
- Menstrual cycle does NOT relates well with --- Estrous profile
- NOT true of partial mole --- Rarely progresses to persistent trophoblastic d/s.
- Mifepristone is NOT used in treatment of --- threatened abortion, ectopic pregnancy, trophoblastic d/s
- NOT an evidence based t/t of menorrhagia --- Ethamsylate.
- Hypertension in pregnancy with renal failure does NOT leads to --- Fetal macrosomia.

- HRT is NOT beneficial in --- Coronary artery d/s.
- NOT given in post menopausal syndrome --- Calcitonin.
- NOT used in hysteroscopy --- Oxygen.
- NOT an indication to perform oral GTT to diagnose GDM---
Hx of eclampsia.

CLINICAL VEGNETTES

- A 55 year old female presents to gynaec OPD with complaints of post-menopausal bleeding for 3 months. O/E there is a gross lesion measuring 10mm x10 mm on anterior lip of cervix. The most appropriate investigation for this patient would be

[AIPGMEE'2003]

- A. Pap smear
 - B. Punch biopsy
 - C. Endocervical curettage
 - D. Colposcopy
- (Ans.B.Punch biopsy)

- Punch biopsy is indicated in grossly visible lesion to rule out malignancy

- A 49 year old female presents to gynae OPD with complaints of post-coital bleeding. O/E her cervix bleeds on touch. Pap smear showing severe dysplasia. What is next step in m/m of this patient

[DNB HRH Delhi'2008]

- A. Cervical biopsy
 - B. Dilatation and curettage
 - C. Endometrial biopsy
 - D. Hysterectomy
- (Ans.A.Cervical biopsy)

1. What is the most probable diagnosis-----Cervical cancer
2. What is the next step in m/m-----Cervical biopsy
3. Definitive t/t in this condition----Hysterectomy

Diagnostic clues are

- As this is a case of post coital bleeding, most likely diagnosis is --- Ca cervix
To confirm the findings of pap smear--- cervical biopsy should be done
- If cervical biopsy confirms Ca cervix --- Hysterectomy and further m/m acc/to stage.

- A 32 year old woman complains of pain during her periods and bluish discolouration of skin over lower abdominal area which increases during her menses. She has history of previous LSCS. Most likely diagnosis is

[DNB HRH Delhi' 08]

- A. Adenomyosis
- B. Myoma
- C. Endometriosis
- D. DUB

(Ans.: C. Endometriosis)

- A 17 year old girl presented to the outpatient department with complaints of primary amenorrhea. She has bilateral inguinal hernia with normal secondary sexual characters without development of pubic hair. Ultra-sound pelvis revealed absent uterus and ovaries. What is the most likely diagnosis? [AIIMS May'06;AIPGMEE '08,'12]

- A. Mullerian agenesis
- B. Turner Syndrome
- C. Androgen insensitivity Syndrome
- D. STAR Syndrome

(Ans.C. Androgen insensitivity Syndrome)

- *Testicular feminization* is char/ by lack of axillary and pubic hairs, absent uterus and upper vagina (Vaginal pouch present) but normal breast development. Full sexual development is achieved by 18-20 years of age. Also k/as Androgen insensitivity Syndrome. Effects of androgens do not manifest in the patient → No axillary and pubic hairs

B/L inguinal hernia is nothing but presence of testes in inguinal region.

- *RMKH Syndrome* is char/ by eugonadotrophic primary amenorrhea, absent/ non-functional uterus and vestigial vagina. Ovulation and secondary sexual characters are normal (normal breast) since ovaries are functional.

- *Turner's Syndrome* is char/ by primary amenorrhea + lack of secondary sexual characters (no breast development).

- *STAR Syndrome* is a rare X-linked syndrome characterized by Syndactyly (webbed) toes, Telecanthus Anal and Renal-genital and malformations.

- A 13-year-old young girl presents in the casualty with acute pain in the lower abdomen. She has history of cyclical pain for last 6 months and she has not attained her menarche yet.

On local genital examination, a tense bulge in the region of hymen was seen. The most probable diagnosis is:

[AIIMS May' 2006]

- A. Rokitansky Küster Hauser syndrome
- B. Testicular feminization syndrome.
- C. Imperforate hymen
- D. Asherman's syndrome.

(Ans.: Imperforate hymen)

Diagnostic clues

Imperforate hymen causing hematocolpos is observed in young girls. These girls present with colicky abdominal pain which is often cyclic. Menarche has not yet set in. However secondary sexual characters are well developed. Vagina gets distended with the menstrual blood and becomes tense. O/E a bluish bulging membrane is recognized.

Sheehan Syndrome is post partum pituitary necrosis. It is d/t ischemia following obstetrical blood loss causes hypopituitarism, failure of lactation is seen.

- A 17 year old girl presented to the outpatient department with complaints of primary amenorrhea with developed breast and normal external genitalia. What is the most likely diagnosis?

[AIPGMEE 2010]

- A. Mullerian agenesis
 - B. Turner Syndrome
 - C. Sheehan Syndrome
 - D. Rokitansky Küster Hauser syndrome
- (Ans.: D. Rokitansky Küster Hauser syndrome)

See above qn

- 19 yr old patient came to the OPD with complaints of primary amenorrhoea. She had well developed breast & pubic hair. However there was absence of vagina. Most likely diagnosis is.

[AIPGMEE'12]

- A. Mullerian agenesis
 - B. RKHS
 - C. Turner Syndrome
 - D. Sheehan Syndrome
- (Ans.: D. Rokitansky Küster Hauser syndrome)

- A lady presented to the outpatient department with secondary amenorrhea after spontaneous abortion. Serum FSH levels are 6 mIU/mL. What is the most likely diagnosis?

[AIPGMEE 2010]

- A. Ovarian failure

- B. Uterine synechie (Asherman syndrome)

- C. Sheehan Syndrome

- D. Fresh pregnancy

(Ans.: D. Fresh pregnancy)

Normal value of FSH is 1-10 IU/L in early follicular phase.

Asherman's syndrome is common after induced abortions.

So answer of exclusion is D.

See above qn

- A 35 year old nulliparous women with primary infertility presents with adenexal mass and CA-125 level of >60 U/mL. What is the most likely diagnosis?

[AIIMS May'2010]

- A. Ovarian cancer
 - B. Endometrioma
 - C. Borderline ovarian tumour
 - D. Tuberculosis
- (Ans.: D. Tuberculosis)

Tuberculosis is the **m/c** cause of primary infertility with adenexal mass in India. CA 125 c/b raised. Ovarian cancer or borderline tumours of ovary are rare cause of primary infertility. Distension of abdomen, ascites, and pain abdomen are common presenting features in these situations.

Endometrioma is a/w cyclical pain.

Clinical condition	Age/parity	Clf	CA 125
Ovarian Ca	Elderly, nulliparity	Abdominal distension, mass abdomen	↑ in 50% of epithelial tumours
Borderline ovarian tumours	Middle age		Normal
Endometrioma	Middle age	Painful adenexal mass, 1 ^o infertility	↑ in > 80%
TB	Any age	Painless adenexal mass 1 ^o infertility	May be ↑

- A 40-year-old female presents with abdominal distension, dyspnea, and weight loss. She is found to have ascites, and raised CA-125. What is the most likely clinical diagnosis?

[AIPGMEE 2012]

- (A) Ca ovary

- (B) Ca cervix
 (C) Ca endometrium
 (D) Genitourinary TB
 (Ans.: (A) Ca ovary)

Distension of abdomen, ascites, weight loss and pain abdomen are common presenting features of ovarian cancer which is further supported by raised CA-125 levels.

D/d of infertility in adenexal masses

Clinical condition	Age/parity	Af	CA 125
Ovarian Ca	Elderly, nulliparity	Abdominal distension, mass abdomen	↑ in 50% of epithelial tumours
Borderline ovarian tumours	Middle age,		Normal
Endometrioma	Middle age	Painful adenexal mass, 1 ^o infertility	↑ in > 80%
TB	Any age	Painless adenexal mass 1 ^o infertility	May be ↑

OPHTHALMIC EXAMINATION/METHODS

OPHTHALMOSCOPY

Distant Direct

- Performed at a distance of 22 cm (20-28 cm range)
- Light is thrown with plane mirror

Direct

- Performed at a distance of 1.57 cm (In normal eye) and 2.33 cm (In aphakic eye).
- Image is 15 times magnified virtual & erect.
[Calculation: Magnification = power/4 = 60/4 = 15]
- Field of observation < field of illumination

Indirect

- Done at 1 m distance (lens is placed 10 cm in front of eye)
- Image is 5 times Magnified, Real (True), Inverted
- Ora serrata, vitreous base, periphery of retina, moving floaters can be visualized, (but fovea is NOT seen)
- Field of observation > field of illumination
- IOC in RD.

Bimicroscopic

- Both central + peripheral part of fundus are visualized
- For D/g of Macular lesions (cyst, neovascularization, maculopathy in NPDR).
- Goldman's / Hruby lens (58.6D), high spherical IOD lens (+78, +90 D) are used along with slit lamp.

Important mnemonics to remember above :

- D=2, I=1 so Direct ophthalmoscopy done at--- approx 2 cm distance
Distant Direct at ---approx 22 cm distance; Indirect at ---approx 1 m distance]
- Image in Direct ophthalmoscopy is Erect, Virtual, and Magnified remember with mnemonic **DEVi Ma**
- Image in Indirect ophthalmoscopy is Magnified 5 Times, Real and Inverted.
remember with mnemonic **MRI In 5 Thousand=**

- Slit lamp + contact lens is useful for examination of --- vitreous, aqueous, cornea, lens
- Slit lamp is the best investigation method for --- diagnosis of vitreous opacities
- Indirect ophthalmoscopy is best for visualization of fundus particularly periphery of retina (e.g. RD) upto ora serrata.
- Functional assessment of optic nerve is done by--- perimetry
- Ophthalmodynamometry is useful in differentiating CRVO from carotid artery emboli
- Tests for acuity of vision are --- Snellen's chart, Log MAR scale, ETDRS etc.
- Acuity for distant vision is tested by --- Snellen chart
- Acuity for near vision is tested by --- Jaeger type cards.
- Colour blindness is tested by --- Ishihara chart / plates (e.g. in d/s of macula or optic nv)

Retinoscopy

Objective method of refraction. Done with plane mirror at 1m distance.

- Reflex moves in same direction (or with the movement of mirror) in--- emmetropia, hypermetropia & myopia < 1D
- Reflex moves in opposite direction in --- myopia > 1D (against movement of mirror)
- No movement of red reflex --- myopia of 1D

Methods of estimating the visual fields

Peripheral field charting Central field charting

1. Confrontation method 1. Campimetry / scotometry using Bjerrum's screen
2. Perimetry (Lister's Goldman's automated) 2. Goldman's perimetry
3. Automated

- Field of vision is tested by --- Perimetry, Bjerrum's screen, confrontation method.
- For detail study of central field of vision & blind spot --- Campimetry (using Bjerrum's screen)
- Peripheral field of vision is least in the upward direction (50°)
- Visual field defects are best detected by Goldman's kinetic perimetry
- Keratometry or ophthalmometry is an objective method for estimating the corneal curvature.

- Confrontation test is a rough method in which the patient's visual field is compared with that of the examiner.

Assessment of Visual acuity in children

Age group	Methods
< 6 mo.	Response to occlusion, VER, optokinetic nystagmus
6 - 18 mo.	Boeck candy beads, Stycar, Teller, Cardiff
18 mo. - 3 yr	Cardiff, Kay picture test, Sheridan-Gardiner,
3-5 yr	Kay picture, Allen/LEA, Glasgow, Snellen, HOTV, tumbling E, stycar test.
>5 yr	LogMR

Macular function tests are

- Cardboard test (two light discrimination test)
 - Amsler grid chart
 - Maddox rod test
 - Entopic view test
 - Laser interferometry, Flying corpuscle test, potential Vn acuity meter (in eyes with opaque media)
- (Remember with mnemonic: CAMEL - Fir Pyasa)

Fincham's test

- It differentiates coloured halos of acute congestive glaucoma from that of acute conjunctivitis
- It also differentiates cataract from acute congestive glaucoma (no breaks in halos)
- In senile immature cataract, test reveals splitting of halos and then reunion

→ In mucopurulent conjunctivitis halos disappear after cleaning of eye

Gonioscope

- The angle of anterior chamber (AC) can be examined with the help of a gonioscope and slit lamp.
- Koeppe gonio lens is most popular type.
- Shaffer's, Scheie's, and RP centre gonioscopic grading are used for grading the angle of AC.

Anterior chamber of eye is:	
Shallow in	- At extremes of ages - In Closed \angle glaucoma - High hypermetropia - Posterior-dislocation of lens - keratoglobus
Deep in	- High myopia - Buphthalmos - Aphakia - Subluxation of lens
Unequal in depth	- Iridocyclitis (shallow at the periphery and deep in the centre) - Anterior synechia

Tonometry

- Tonometer – is used for accurate determination of IOT
- Schiotz-tonometer is m/c used for indentation tonometry

→ *Applanation tonometry records the IOT more accurately as it eliminates factor of ocular rigidity*

→ *Tonography – is non-invasive technique for determining aqueous flow (C-value)*

- Visual axis:** A line perpendicular to a tangent to the cornea through the centres of the lens & the fovea of retina.
- Alpha angle:** The angle between the visual and the optic axes as they cross at the nodal point of the eye.
- Kappa angle:** The angle formed by pupillary axis and visual axis at the pupil.

ERG (Electroretinogram)

- Action potential generated in retina is recorded. It reflects electrical activity of photoreceptor cells and bipolar cells of retina.
- A wave in ERG is produced from photoreceptor layer (rods & cones) of retina.
- ERG is Negative in --- retinoschisis, congenital stationary night blindness.

EOG (Electrooculogram)

- Activity of pigment epithelium is recorded.
- Arden index** or ratio is ratio b/w light peak to dark trough. Normally it is 1.85

VEP (Visual evoked potential)

- EEG at occipital lobe. Activity recorded beyond ganglion cells upto outer occipital.

SOME IMPORTANT OPHTHALMIC FINDINGS

Finding	Causes
Metamorphsia (Rainbow Vn)	Central serous choroidal retinopathy, Senile macular degeneration, macular hole
Tubular Vn	RP, glaucoma (chronic simple type), hysteria, quinine
Red Vn	Ethambutol toxicity (Red remains, green goes)

Roth spots

White centered retinal h'ages in

- Leukemia
- SABE
- DM [Mn: LSD]

Cytoid Bodies

- Papilledema
- Infective Endocarditis
- SLE
- AIDS [Mn: PISA]

Salt pepper fundus

- Syphilis
- Rubella
- Baton Mayors synd
- Leber's amaurosis

Follicles

- Trachoma
- Adeno viral/Follicular conjunctivitis [Mn: fAT]

Floaters

- Vitreous h'mge
- RD
- Chorioretinitis uveitis
- Myopia

Papillae

- Trachoma
- Spring catarrh
- Allergic conjunctivitis (soft contact lens users)
- Giant papillary conjunctivitis [Mn: GAST]

Coloured Halo

Corneal edema is the basic pathology

- Mucopurulent conjunctivitis
- Glaucoma

Acute closed \angle , Pigmentary, Phacogenic

Epidemic dropsy glaucoma

- Cataract (intumescent stage)
- Uveitis
- Corneal abrasions (contact lens users)

Cherry Red Spot at fundus

D/to ischemia and occlusion of retinal vessels

- CRAO
- Blunt trauma (Berlin edema/ commotio retinae)
- Tay-Sach's disease (90%)
- Niemann pick disease
- Metachromatic leukodystrophy (MLD)
- Multiple sulfatase deficiency
- Goucher's, Sandoff's
- Sialidosis type 1 & 2 [NOT seen in CRVO]

White pupillary Reflex (leukocoria)

- Retinoblastoma
- Pseudoglioma
- Total RD
- Tuberculoma of choroid
- Coat's disease
- Persistent primary vitreous, retrolental fibroplasia
- Retrolental exudate memb.

Ring scotoma

- RP
- Glaucoma (Double arcuate scotoma)

Iris nodule

- Granulomatous uveitis, Gumma of the iris, Leprosy
- Melanoma
- Tuberculoma

Cotton wool spots

- HTN, DM
- Toxemia of pregnancy
- Anemia
- CVD (DLE, PAN, Scleroderma)

ANATOMICAL & PHYSIOLOGICAL CONSIDERATION

Development of Structures of eye

Surface	o Lens
ectoderm	o Epithelium of cornea, conjunctiva, eyelids, lacrimal apparatus
	o Glands – lacrimal, tarsal, conjunctival
	o Skin of the eyelids
Neuro-ectoderm	o Retina with its pigmentary epithelium
	o Epithelium of iris, ciliary body
	o Optic nerve, cup, vesicle
	o Sphincter & dilator pupillae (S/M of iris)
	o Secondary vitreous
Paraxial	o Sclera, ciliary body, iris, choroid
mesoderm	o Muscles---ciliary
	o Stroma of iris, cornea
	o Upper/medial walls of orbit
	o Substantia propria, endothelium of cornea
	o Vitreous (primary)
	o Vascular endothelium

- Stroma/musculature of most structures (mentioned above) is formed by mesoderm
- Lower and lateral walls of orbit are derived from visceral mesoderm
- Extraocular muscles develop from pre-optic myotomes
- Angle of anterior chamber, anterior layer of iris, stroma of cornea develops from mesodermal condensation

Embryological remnants of the eye

- o Mittendorf's dots (of anterior hyaloid artery)
- o Posterior embryotoxon
- o Bergmeister's papilla (remnant of hyaloid artery)
- o Epicapsular stars

Refractive Index and Refractive power

	Vitreous, aqueous	Cornea	Lens Cortex	Lens Nucleus	Lens Average
R.I.	1.33	1.376	1.38	1.40 (Max ^m RI)	1.39
Power		+ 43.78 D			+ 17.75 D

- o Total refractive power of eye is ----- 58 - 60 D (avg 58.6)
- o Total refractive power of reduced eye is ----- -58 to 60 D

- o Total refractive power of cornea is ----- 43.78 +/- 1.86 D
- o Axial length of the globe is 23.57 +/- 1.57 mm
- o Total axial length (AP diameter) of the eye is -----24 mm in adults (But only 17.5 mm at birth).
- o Orbit volume is 24-30 ml.
- o Eyeball volume is 5-7 ml.
- o Depth of anterior chamber of eye: 2-3 mm.
- o Length of optic nerve 4.7 - 5 cm
- o Normal cup (0.5 mm) & disc (1.5 mm) ratio is 1:3
- o Normal AV ratio in funduscopy is 3:4
- o Sclera is thickest at posterior pole near the optic nerve.
- o Sclera is thinnest at just behind the insertion of recti.

→ Total refractive/diopic power of eye is 58.5 D (cornea 40 D + lens 17.75 D + physiological tone of ciliary muscle 1 D)

→ Max^m refractive power --- Anterior surface of cornea (47 D)

→ Maximum refractive index --- Centre of lens (1.40)

→ Lens & cornea are avascular structures of eye. So fluorescein angiography is not helpful in identifying lesions.

Anatomy of orbit

- o Upper tendon (Annulus of Zin) arises from Lesser wing of sphenoid.
- o Lower tendon (Lockwood tendon) arises from Body of sphenoid.
- o Optic foramen is situated b/w Lesser wing & Body of sphenoid. (Remember: Situated between Love & Bailley).

Eye of Newborn & Infants

- o Newborn's eye is short (axial length 17.5 mm.), generally hypermetropic (+2.5D), and the fovea is immature.
- o Visual acuity is approx. 6/60 or 20/400
- o Cornea is relatively large in newborns (averaging 10 mm) and attains adult size (12mm) by 2 yr.
- o Retina is fully developed at birth except at macula
- o Orbit is more divergent (50°) compared to adults (45°).
- o Newborn's eyes are not binocularly coordinated so they do not have binocular stereoscopic vision and have a limited peripheral field of vision.

Stages of binocular vision/ Visual reflexes Fixation

- o At birth → No central fixation, eyes move randomly.
- o At 1 wk → Vestibulo-ocular reflex, optokinetic nystagmus.

- By 1 month → Mono-ocular fixation or conjugate fixation starts developing. She develops a preference for face.
- By 2 month → Fixation well developed. (bifoveal)
- By 3 months → Binocular vision & eye coordination starts.
- By 4 months → Right hemispheric dominance in recognizing faces is shown.
- By 5-6 months → visual reflex formation occurs. Binocular fusional reflexes develop. Menace response, **Macular stereopsis & accommodation reflex** develops.

Fusion

- Corrective fusional reflex, which allows eye to function binocularly even in stress, starts functioning during 1st yr of life and fully established by 5-6 years. By 6 years full visual acuity is attained & binocular single vision is developed.
- Binocular Vn with stereopsis --- by 7 years
 - Critical period for the development of fixation of eye reflexes is 2-4 months.
 - Normal resolution visual acuity reaches adult acuity (6/6 or 20/20) by 6 yrs.
 - Visual acuity is a measure of formed sense.

Lens

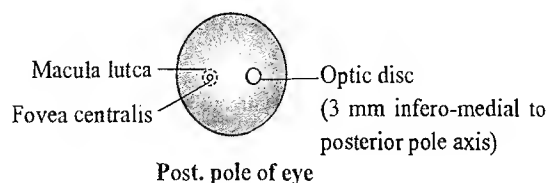
- Lens derives its energy from carbohydrates and structural material from amino acids of aqueous and vitreous.
- Glycolysis is the main route of metabolism of glucose in the lens.
- Lens is devoid of blood vessels & has low metabolic rate.
- Lens contains 60% water and 34% proteins. The physio-chemical arrangement of lens proteins along with electrolytes and SH group provides transparency to the lens.

IOT (Intraocular Tension/Pressure)

- Ranges from 10-20 mmHg. It is most accurately measured by a manometer which is not possible in human eyes.
- Normal mean ocular tension is 15.4 ± 2.5 mmHg by applanometry and 16.1 ± 2.8 mmHg by Schiotz, usually the IOT does not vary significantly between the two eyes.
- Normal diurnal variation is up to 5 mmHg. A consistent difference of 4 to 6 mmHg b/w two eyes is k/as **Downey's sign** and is an indication to investigate for glaucoma.

Fundus examination (FUNDOSCOPY)

- Macula** --- At the posterior pole of eye 3mm lateral to optic disc, there is a yellowish pigmented spot, the macula lutea (where cones > rods)
- In the centre of macula there is rod free depressed portion (where only cones are present) k/as **fovea centralis**. It is the point where visual acuity is maximum. Fovea centralis is the thinnest part of retina
- Optic disc** --- Depressed area of optic disc (physiological cup) contains no rods/cones and is therefore insensitive to light and called physiological blind spot.



- Cones are more in centre and decrease in periphery. Cones respond to bright light and play role in photopic and color Vn.
- In fovea centralis --- only cones (maximum visual acuity) [cones in centre]
- In macula lutea --- cones > rods (photopic Vn)
- In blind spot (physiological cup) --- no rods, no cones
- In periphery --- rods > cones (scotopic Vn)

Important Fundoscopy Findings:

Condition	Fundus
Normal disc	Pink, central pallor
CME (Cystoid macular edema)	"Flower petal"
CSR (Central serous retinopathy)	"Ink-blot, enlarging dot" & smoke stake patterns
CRAO	"Cattle truck" appearance of retinal veins, cherry red spots
Primary optic atrophy	"Chalky white" disc
Consecutive optic atrophy	"Yellow waxy" disc
Sarcoidosis	Candle wax drippings, venous sheathing peri-phlebitis
CRVE, Branch RVO, AIDS	"Cotton wool" spots
Stargardt's macular dystrophy	Beaten-bronze appearance
Chloroquine	Bull's eye maculopathy

REFRACTIVE ERRORS

	Myopia	Hypermetropia
Also k/as	Short sightedness	Far sightedness.
Difficulty in	Distant v/n	Both near and distant v/n are defective
Axial length of eyeball	↑	↓
Power of eye	More	Less
Eyes looks	Large	Small
Byeball	Large	Small
Pupil	Large	Small
Cornea	Megalocornea	Microcornea
Angle of AC	Large	Shallow
Predisposed to	Open angle glaucoma (POAG)	Narrow angle glaucoma
Squint	Apparent <u>convergent</u> squint.	<u>Latent convergent</u> squint
Complications of higher stage	<ul style="list-style-type: none"> - Retinal h'ages, - Vitreous h'age - Lattice degeneraⁿ & subsequent RD/ R. tears - Complicated cataract, POAG - <u>Foster Fuch's spots</u> at macula 	<ul style="list-style-type: none"> - <u>Degenerative retinoschisis</u> - Early presbyopia - Choroidal detachment - CRVO - Recurrent styes, blepharitis, chalazion

- *Aphakia* produces high degree of hypermetropia
- *Flat cornea* produces hypermetropia + astigmatism
- Index Myopia is seen in - Nuclear sclerosis, Old age (senile cataract), DM.
- Index Hypermetropia is seen in - Old age (d/t to total decrease in refractive index of lens)
- Change of 1 mm in AP diameter (axial length) of eyeball leads to change of 3 D in the refraction. Shortening causes Hypermetropia & lengthening myopia
- Most important refractive surface of the eye is --- anterior surface of the cornea (cornea-air interface). A decrease in 1 mm in corneal curvature leads to hypermetropia of 6D
- Frequent changes of presbyopic glasses is an early symptom of --- Primary open angle glaucoma

- *Constantly changing refractive errors* (Frequent change of presbyopic glasses) is seen in :-

1. Intumescent cataract
2. Late glaucoma
3. Diabetes

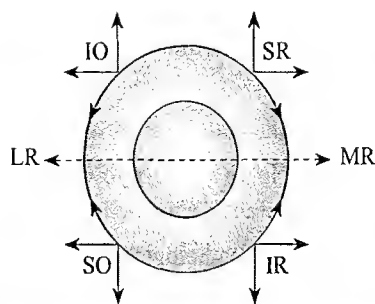
MYOPIA

- Physiological myopia is the m/c eye disorder worldwide.
- Posterior staphyloma can cause pathological myopia.
- *Pathological myopes* may present with ↓ed visual acuity, an unusually large exophoria, strabismus (typically exotropia), open angle glaucoma, premature lenticular opacification and ↑ed axial length (26.533.5mm).
- *Fundus examination* may unveil any of these signs: flat, obliquely inserted discs, posterior staphyloma, a myopic crescent, patchy choroidal atrophy within the posterior pole, vitreous syneresis, breaks in Bruch's membrane with accompanying choroidal atrophy k/as **Lacquer cracks** (usually manifest in young males), subretinal neovascular membrane with overlying retinal pigment epithelial hyperplasia (**Fuch's spot**), subretinal scarring, bleeding, exudate and retinal breaks or RD (retinal detachments).
- *Progressive myopia* is a/w systemic d/s such as Marfan's syndrome, retinopathy of prematurity, Ehler's-Danlos syndrome, Stickler's syndrome and albinism.

HYPERMETROPIA

- Hyperopia, commonly k/as being farsighted or longsightedness.
- It results from the eyeball being too short.
- *Signs of hypermetropia*
Small eyes, cornea smaller, anterior chamber is shallow, small optic disc, shot silk retina, short AP length of eyeball.
- Axial Hypermetropia is commonest form. There is axial shortening of eye ball 1mm=3D.
- Curvatural hypermetropia- Curvature of cornea/lens flatter 1mm ↑se = 6D
- Index hypermetropia ↓se in refractive index of lens also seen in **Diabetes**.
- In children, severe hyperopia can cause them to "over-focus", leading to double vision (diplopia), Crossed eyes (strabismus) & lazy eye (amblyopia). Blurred vision, **asthenopia**, accommodative dysfunction, binocular dysfunction also seen.

EYE MUSCLES



	Primary action	Synergist	Antagonist	Yolk/Muscle
SR	[Elevation]	IO, MR	IR, SO	IO of opp. eye
IR	[Depression]	SO, MR	SR, IO	SO "—" "
SO	[Intorsion]	IR, LR	IO, SR	IR "—" "
IO	[Extorsion]	SR, LR	SO, IR	SR "—" "
MR	[Adduction]	SR, IR	LR, SO, IO	LR "—" "
LR	[Abduction]	SO, IO	MR, SR, IR	MR "—" "

Superiors are intortors

- ➔ **Inferior oblique (IO)** is the only extrinsic m/s of eye which does not take origin from annulus of Zinn. (It arises from lower & inner orbital wall near lacrimal fossa, i.e. orbital plate of maxilla)
- ➔ In isolated eyeball, IO is the m/s which helps in recognizing side of eyeball (right or left)
- ➔ Muscles of marriage --- MR, Muscles of divorce --- LR, and Copying muscles are --- SO.
- ➔ Longest EOM → SO
- ➔ In the lesion of m/s, diplopia is towards the action of m/s. For example in SO palsy diplopia is on looking down.
- ➔ **Spiral of Tillaux** - An imaginary line connecting the insertion of recti m/s. Insertion of MR is closest to the corneal limbus.
- ➔ Distance of MR from sclero-corneal junction -- 5.5 mm

OPHTHALMOPLEGIA

Plegia	Paralysis of	Causes
1. Internal ophthalmoplegia	Intrinsic m/s (ciliary, iris)	Multiple sclerosis (M/c), DM (unilateral) Diphtheria, Lesions of MLF + 6th CN nucleus
2. External ophthalmoplegia	Extra-ocular m/s	Lesions at oculomotor nucleus, Diphtheria
3. Cycloplegia	Sphincter pupillae ↓ Mydriasis	Diphtheria, Trauma, Syphilis, Meningoencephalitis, Methyl alcohol, atropine

- **Spasm of accommodation** is d/to ↑ ciliary muscles tone (>>1D) leading to → Miosis. Seen in young myopes engaged in near work, with the use of strong miotics. T/t is atropine.
- In thyrotoxic exophthalmos inferior rectus muscle is first to be involved :-
IR → MR → SR → LR
- In Myasthenia gravis, 1st m/s involved is LPS.
- **Superior orbital fissure syndrome** is total ophthalmoplegia d/to involvement of 3,4,6th CN.
- **Orbital apex syndrome** is superior orbital syndrome + optic nerve involvement.
- First sign of cavernous sinus involvement/ raised ICT is 6th CN palsy.
- CN which pass along the wall of cavernous sinus 3,4,5,6.
- CN which pass through the body of cavernous sinus is 6th CN.
- Structures passing through optic foramen are --- Optic nerve & ophthalmic artery.
- **Ocular myoclonus** is rapid horizontal oscillatory nystagmus + movements of palate d/to damage in tegmentum of midbrain.
- **Opsoclonus** is irregular jerky saccadic movements varying in direction d/to cerebellar lesion. An important sign of **neuroblastoma**, encephalitis, trauma, paraneoplastic syndrome.
- **Sherrington's law of reciprocal innervation** states that during ocular motility, ↑ed contraction of an extraocular m/s is accompanied by ↓ed contractility of its antagonist.

Ocular movements are restricted / painful in

- Pan-ophthalmitis
- Posterior uveitis
- Retrobulbar optic neuritis --- pain more on upward movement
- Iridocyclitis (pain worsening at night)

Oculomotor nerve palsy

- **Ptoxis** with diplopia
- **Pupillary sparing type**: Oculomotor nerve palsy with **pupillary reflex sparing** is seen in DM, hypertension
- **Pupil involving type**: Mydriasis is seen, unresponsive to both light (loss of light reflex) and accommodation. Seen in PCA aneurysm.
- Lateral gaze --- **eye down & out**
- 3rd CN may be injured in ciliary ganglion damage (HZV, Influenza), ischemia (DM/Temporal arteritis).

Trochlear nerve palsy/ SO palsy

- Hypertropia + excyclotorsion
- **Vertical diplopia** (diplopia on reading/looking down)
- Tested by 'head tilt'.

- Vertical diplopia is seen in → Trochlear nerve palsy.
- Vertical gaze palsies are d/to damage to pre-motor structures in the midbrain, namely the rostral interstitial nucleus of the MLF and the interstitial nucleus of Cajal.
- Vertical nystagmus is seen in → Pons, brainstem lesions.

Abducent nerve palsy/ LR palsy

- Lateral rectus is paralyzed resulting in **horizontal diplopia** (which worsens on gazing to the side of lesion) E.g. Left 6th CN palsy leads to diplopia in left gaze
- Causes are --- ↑ ICT, supratentorial mass lesion over petrous, # base of skull

- Bielschowsky sign is for superior oblique palsy.
- Abducent nerve is m/c injured nerve in raised ICT.

Lesions in optic pathway

Lesion of	Effects
1. Optic tract	Incongruous homonymous hemianopia
2. Optic radiation	Homonymous hemianopia (Can be incongruous or congruous)
3. Optic chiasma	Bi-temporal hemianopia (D/to tumours. e.g. prolactinoma)
4. Visual cortex	Total hemianopia (d/to PCA occlusion) → Cortical blindness Homonymous hemianopia (Always congruous) 1. Inf fibres of temporal lobe, Meyer's loop → Pie in sky, upper quadrantanopia 2. Sup. fibres of parietal lobe → Pie in floor, lower quadrantanopia
6. Occipital stroke	Hemianopia with macular sparing (Blood supply is maintained by MCA in upper part)

- 1st order neurons in optic pathway → Rods & cones.
- Quadrant hemianopia (Quadrantanopia) are d/to lesion in → Temporal lobe.
- Vitamin B12 (cobalamin) deficiency should be considered in the d/d of any patient with optic nerve cupping, normal IOP and bitemporal visual field loss.

Supranuclear palsy

- Also k/as Steele-Richardson-Olszewski syndrome, is a neurodegenerative d/s
- Presentation : An old man with hx of repeated falls &

vertical gaze palsy.

- **Progressive supranuclear palsy (PSP)** is a rare brain disorder that causes serious and progressive problems with control of gait and balance.

NYSTAGMUS

Nystagmus is rhythmic oscillations of eye d/to vestibular or optokinetic stimulation

Nystagmus	Lesion of	Causes
1. Horizontal	Vestibular/ labyrinth	Gazed to opposite direction (COWS)
	Cerebellar	Gazed to same direction, past pointing is seen
2. Vertical upbeat	Pons, Posterior fossa	Phenytoin, Posterior fossa lesion
3. Vertical downbeat	Posterior fossa	Arnold-Chiari malformation Cervicomedullary tumours, Lithium, Cerebellar atrophy
4. Visual cortex		Total hemianopia (d/to PCA occlusion) → Cortical blindness Homonymous hemianopia (Always congruous) 1. Inf fibres of temporal lobe, Meyer's loop → Pie in sky, upper quadrantanopia 2. Sup. fibres of parietal lobe → Pie in floor, lower quadrantanopia
6. Occipital stroke		Hemianopia with macular sparing (Blood supply is maintained by MCA in upper part)

- Irritative lesion of labyrinthine exceptionally causes nystagmus to the same side
- Congenital blindness resulting from anterior visual pathway lesion causes complex, searching nystagmus with irregular, pendular (sinusoidal), jerky features
- Nystagmus may be pendular (amblyopia), jerky, (vestibular), rotary (labyrinthine), horizontal (cerebellar), vertical (brainstem).
- Pathological nystagmus d/to sensory deprivation (any cause of opaque media) always produce pendular nystagmus.
- Pontine paraventricular formation (PPRF) is horizontal gaze centre.

- Sea-saw nystagmus of Maddox

Found in para-chiasmal lesion (e.g. Craniopharyngioma).
So a/w bitemporal hemianopia.

- *Rapid rotatory nystagmus*
Miner's nystagmus
- *Ataxic nystagmus*
Is d/to motor imbalance. Seen in internuclear ophthalmoplegia.e.g. multiple sclerosis, sarcoidosis, (lesions of MLF + PPRF abducent nu.).
- *Optokinetic nystagmus*
Physiological nystagmus seen in travel in train. Pursuit & saccadic movements are seen. M/c d/to parietal lobe lesion.. Used to test malingers, testing V_A in very young..
- *Drugs*
Sedative, anti-convulsants(dilantin), alcohol, lithium
- *Latent nystagmus*
Seen in infantile esotropis (convergent squint). Manifests on cover-uncover test.
- *Saccadic movements are abrupt eye movements to fix the object on fovea.*
- *Spasmus nutans are head nodding movements in dim light. Seen in children.*

PUPIL

- Constrictor pupillae is s/by : Short ciliary nerves, post ganglionic fibres from ciliary ganglion.
- Dilator pupillae is s/by : post ganglionic parasympathetic fibres from EWN (of oculomotor nerve).

Adie's Pupil

- Tonic pupil which dilates with atropine instillation and constricts with pilocarpine instillation.
- Seen in healthy young women a/w mild dysautonomia.
- Seen in ---**Shy Drager syndrome**, Segmental hypohidrosis, DM, Amyloidosis.
- Pupillary light reaction is very sluggish or absent.
- Typically **large dilated pupil** d/to cholinergic supersensitivity (denervation hypersensitivity)
- Near reflex is slow and tonic
- Accommodation reflex is also slow.

Argyll - Robertson pupil

- Light reflex - nt. & near or **Accommodation Reflex Present** (ARP). Light near dissociation.

- Seen in **neurosyphilis**, DM, syringomyelia, disseminated sclerosis
- Pupil is **small , irregular (miotic pupil)** & asymmetrical.
- Atropine instillation does not dilate pupil.
- Visual acuity is normal.
- Both direct and consensual light reflex are absent, but accommodation (near) reflex is normal.

Horner's syndrome

- Horner syndrome is a triad of :
Miosis (D/to sympathetic loss) +
Ipsilateral ptosis (D/to lesion of Muller's m/s) +
Enophthalmos (Apparent enophthalmos)
& **anhidrosis** (reduced ipsilateral sweating).
- Most cases are idiopathic, but it could be d/to brainstem lesions, carotid dissection, or neoplasm compressing upon the sympathetic chain (E.g., Pancoast tumour).
- Loss of cilio-spinal reflex (Normally when we pinch at the nape; pupil dilates)
- *Heterochromia irides* is seen in congenital H~ (<2yr). The affected iris is blue while other iris changes to brown. Iris pigmentation is under sympathetic control during development, which is completed by age 2 years. Heterochromia is uncommon in patients with Horner syndrome acquired later in life

It is enophthalmos that is seen rather than exophthalmos

Pupil in

- Acute congestive glaucoma – mid dilated, vertically oval, non-reacting
- Absolute glaucoma – dilated pupil with painful, blind eye
- Acute conjunctivitis – normal briskly reacting
- Acute anterior uveitis – Constricted, irregular & sluggishly reacting.
- *Unequal pupils in eyes is suggestive of --- Glaucoma*
- *First sign of optic nerve lesion or d/s --- Afferent pupillary defect.*
- *Marcus Gunn pupil is diagnostic of --- Acute retrobulbar neuritis (optic neuritis).*
- *Abducent nerve is m/c injured nerve in raised ICT*
- *Oculomotor nerve palsy with pupillary sparing is seen in DM*

Pupillary reactions

Various type of pupillary reflexes (reactions) and their examples are given below:-

	Reflex	Feature	Seen in
Normal	Light reflex		
	Near reflex	Convergence	
		Miosis	
		Accommodation	
	Psychosensory reflex	Pupil dilates in anxiety	
Abn	RAPD (Relative afferent pupillary defect)	Marcus Gunn pupil	Retrobulbar neuritis
	TAPD (Total afferent pupillary defect)		Optic atrophy
	Holme's Adies pupil/tonic pupil	Mid dilated pupil	Lesion of ciliary ganglion & short ciliary nerve.
	Light near dissociation	ARP	Neurosyphilis

VISUAL CYCLE

Visual Cycle

- Visual impulse is a/w --- The condensation of opsin with vitamin A aldehyde (retinal)
- Visual phototransduction is a process by which light signals are converted into electrical signals in rod cells, cones, and ganglion cells of retina.

Parvocellular Pathway

- Located on layers 3,4,5,6 of retina
- Carries signals for colour vision, texture, shape of object and fine details.

Magnocellular Pathway

- Located on layers 1 and 2 of LGB or lateral geniculate nuclear laminae
- Carries signals for detection of movement, depth and flicker
- It receives signals from M - cells

Blobs

Are cluster of cells arranged in mosaic in layers 2,3 of visual cortex. They are concerned with colour vision.

Role of

- Amacrine cells** - are interneurons in the retina. Amacrine cells are responsible for 70% of input to retinal ganglion cells. Color & luminosity under changing light conditions is regulated by amacrine cells.
- Bipolar cells**: Retinal bipolar cells are interneurons that form a part of the direct visual information from a light source to the brain.
- Ganglion cells**: are the first neurons in the retina that respond with action potentials. (Final output neurons from retina)

CONJUNCTIVA

Conjunctivitis

- Pink eye** is caused by *H.influenzae* (acute bacterial conjunctivitis) and adeno virus
- M/c** cause of viral conjunctivitis --- adeno virus.
- M/c** cause of severe keratoconjunctivitis in contact lens user --- *Acanthamoeba*.
- M/c** carcinoma of conjunctiva --- SqCC.

Neonatal Conjunctivitis

- Neonatal conjunctivitis** can be caused by *N. gonorrhoeae*, staph, chlamydia, diplococcus (except strepto).
- M/c** cause of conjunctivitis in neonates within 24-48 hours --- Chemical conjunctivitis d/to $AgNO_3$
- M/c** cause of bilateral conjunctivitis in neonates within 3-5 days --- *Neisseria gonorrhoeae*. Most common complication after neonatal gonococcal conjunctivitis is dacryocystitis.
- M/c** cause of bilateral conjunctivitis in neonates after 7 days --- *Chlamydia trachomatis*

Herpes Simplex infection of the Eye

- HSV-I affects mouth, lips and the eye (vesicles around lips / orbit) while HSV-II affects essentially ano-genital region.
- CL/f**:
 - Blepharoconjunctivitis / acute follicular conjunctivitis
 - Initial corneal lesion is a superficial punctate keratitis
 - Severe form
 - Punctate keratitis leads to **dendritic keratitis/ ulcers** which are pathognomonic.
 - Disciform keratitis (**discoid disc**) may develop
- In exudative choroiditis patient often complains of flashes of lights (photopsia)

- Pathognomic feature of viral keratitis --- ↓ed corneal sensation.
- *Recurrent infection causes*
 - The **most characteristic lesion** of HSV recurrent infection is the **dendritic ulcer (dendritic keratitis)**
 - Punctate epithelial keratitis (initial lesion)
 - Geographical ulcer (when dendritic ulcer enlarges and becomes amoeboid)
 - Disciform keratitis (due to hypersensitivity).

TRACHOMA

- Also k/as **Egyptian Ophthalmia**
- Trachoma is a leading preventable cause of blindness.
- Screening age group for trachoma 5-9 yrs.
- **"SAFE"** strategy used for trachoma is
Surgery to correct trichiasis of lids
Antibiotics (Oral azithro/ topical tetra) for acute infection
Facial hygiene
Environmental change
- **Follicles** are seen.
- Trachoma bodies (elementary bodies) are stained with Lugol's iodine, Giemsa, & methyl green pyronin.
- Blanket therapy (Mass t/t) is done by using azithromycin if prevalence of trachoma follicles in 1-9 yrs population are >10% (WHO) or >5% (India, acc/to Park's).

→ *Conjunctival follicles (follicular conjunctivitis) are seen in trachoma, benign folliculosis, acute and chronic follicular conjunctivitis*
[Mnemonic : T-BACT]

Vernal KC (VKC) or Spring catarrh

- Recurrent, bilateral, interstitial, self limiting, allergic inflammation of conjunctiva having seasonal incidence more common in *summer*
- D/to *hypersensitivity reaction* to some exogenous allergens
- Seen in age 4-20 years and $M > F$.
- **CI/f**
Marked burning and itching sensation which accentuate in warm atmosphere, lacrimation, string or ropy discharge
 - **Palpebral form** – upper tarsal conjunctiva involved.
Papillae are hard, flat topped arranged in 'cobblestone' or 'pavement stone fashion'
 - **Bulbar form** – Dusky red triangular congestion. Discrete red dots around the limbus k/as **Tranta's spots** (Consist of eosinophils + epithelial debris)

- T/t: Cold compresses, oral antihistaminics & frequent instillation of medrysone (cortisone) eye drops provides symptomatic relief.

Important conjunctivitis

Conjunctivitis	Etio	C/F and T/t
Angular	Moraxella Axenfeld/ lacunata (gram-ve diplobacillus)	Zn oxide + tetra
Classic acute membranous	<i>Corynebacterium diphtheriae</i>	
Pseudo-membranous	<i>Adenoviruses, Staph., Strepto/pneumo-/gonococci, HSV, chlamydia, E.coli, erythema multiforme, SJS</i>	
Mucopurulent	Staph. aureus	
Swimming pool	Chlamydia trachomatis serovar D-K	Acute inclusion conjunctivitis
Epidemic KC	Adenovirus 8, 19	
Pharyngo-conjunctival fever	Adenovirus 3, 4, 7	
Acute haemorrhagic / Apollo	Picornaviruses (Coxsackie A ₁₄ , Enterovirus -70), Adeno 11, 37	Contagious, punctate keratopathy+
Neonatal	Chlamydia trachomatis	
Phlyctenular	Allergic, d/to endogenous bacterial proteins mostly tuberculous	Ring ulcers +
Vernal /Spring catarrh	Seasonal allergic conjunctivitis hypersensitivity to exogenous allergen	Ropy discharge + Papillae + (but no follicles), Horner-Tranta dots are seen in bulbar form

CORNEA

Cornea Plana	Phthisis bulbi
Microcornea	(<10mm horizontal diameter) Microphthalmos, Phthisis bulbi
Megalocornea	(>13mm) Buphthalmos

- Corneal transparency is maintained by --- Descemet's membrane (Endothelial lining).

- Corneal curvature is more important for focussing
- Cornea gets its nourishment from atmospheric oxygen and from the superficial plexus formed by episcleral branches of anterior ciliary arteries (annular plexus). Cornea has no blood vessels of its own. It is nourished by aqueous humor.
- **Primary herpetic infection** is found in non-immune subjects. Its incidence ↑es with age.
- Endothelial ionic pump of the cornea c/b blocked by inhibition of anaerobic glycolysis.
- Corneal epithelium : Stratified SqE.
- Donor cornea from cadaveric eye c/b used 6 hrs of death. It is stored in Mc Kaufmann's media for 4 days.
- *Schwalbe's line* is the anatomical line found on the interior surface of the eye's cornea, and delineates the outer limit of the corneal endothelium layer. Superficially it represents the demarcation b/w the cornea and the sclera; the endpoint of Descemet's membrane. Seen in angle of anterior chamber.

Ix for cornea

- *Pachymetry* : Measures corneal thickness.
- *Keratometry* : Detects changes in corneal curvature.
- *Placido's disc* : To assess corneal surface
- *Specular microscopy* : To examine corneal endothelial cells.
- *Loss of corneal sensations occur in — Viral/herpetic Keratitis, neuromyolytic keratitis, leprosy, absolute glaucoma, DM.*
- *Blurring in underwater is d/to ↓refraction of cornea.*
- *Fascicular ulcer (ring ulcer) — is seen in Phlyctenular keratitis (e.g. in TB)*
- *Numular keratitis is seen in herpes zoster ophthalmicus.*
- *Sclerosing keratitis is seen in scleritis.*
- *Ulcer serpens — is pneumococcal hypopyon ulcer*

Corneal Ulcers

- Inverted comma hypopyon corneal ulcer is d/to -- Pneumococcus.
- "**Ulcer serpens**" is d/to -- Pseudomonas.
- Chemical cautery of corneal ulcer is done by --- Trichloroacetic acid or carbolic acid.

Fungal Corneal Ulcer (Keratomycosis)

- Mycotic or fungal keratitis is frequently seen in immunocompromised pts of rural areas in tropical countries.

- M/c organisms are : **Aspergillus fumigatus**, Fusarium, candida albicans
- Typically seen after injury from vegetative matter e.g. wooden stick injury
- **CI/f**
 - Slough is dry with feathery borders
 - Hypopyon, **satellite lesions** may also be seen
 - Immune ring of Wsseley
 - Signs >> symptoms
- **T/t**
 - Local natamycin is DOC (amphotericin-B drops, miconazole ointment also useful).

Keratoconus

- Progressive non-inflammatory b/L thinning and bulging of central cornea, which becomes cone shaped
- Usually congenital and a/w — Turner's, Down's, RP, EDS, Atopic dermatitis, Marfan's, blue Sclera [Mnemonic : The DREAMS]
- AR condition, F>M
- **D/g**
In early stage, diagnosed with corneal topography, which demonstrates the cone and typical astigmatic pattern
- **CI/f**
Munson's sign
Fleischer's ring d/to iron deposition in epithelium
Vogt's striae (best seen with slit lamp)
- **T/t**
 - In the early stages, vision may be improved with spectacles but contact lenses are more beneficial as they eliminate irregular corneal curvature, and have supporting effect.
 - If d/s is progressive, keratoplasty (penetrating / full thickness) is most satisfactory t/t.
- *LASIK is absolutely contraindicated in keratoconus or corneal ectasia or when cornea is very thin (thickness is limited to <450 nm) because of risk of endothelial damage*
- *M/c fungus infecting lids — Candida albicans.*
- *Arcus senilis is d/to --- lipid deposition in stroma.*
- *Band shaped keratopathy is d/to --- deposition of Ca⁺⁺.*

Pterygium

- Wing shaped fibrovascular fold of conjunctiva encroaching upon the cornea from either side. Islets of Vogt & Stocker's line are seen on head end.
- More common in hot climate, in elderly males.
- **Stocker's line** : d/to deposition of iron.

- *Pinguecula* is considered precursor of pterygium. There is thickening of bulbar conjunctiva near the limbus in the area of palpebral fissure. A/w ↑ing age & UV rays exposure.

Corneal dystrophies (CD)

- Progressive, hereditary corneal disorders which are b/L symmetrical, non-vascularized, show no signs of inflammation and are without associated systemic d/s.
- Reis Buckler CD is an AD condition.
- Hereditary stromal CD : Common. Occur b/L around puberty. T/t is **penetrating keratoplasty**.
 - Granular/nodular form (Groenouw) : AD
 - Lattice form is AD & is a/w → Amyloidosis
 - Macular form is AR, least common & is a/w → mucopolysaccharoidosis
- Endothelial CD : Rare
 - *Endothelial dystrophy of Fuchs* is m/c endothelial CD. Overall it is a rare variety of CD seen in elderly females. A/w cornea guttate.
- Epithelial CD : Present as recurrent corneal erosions. Treated by pad & bandages.
- Microcystic CD are a/w "Map dot & finger print" appearance

Staphyloma

Staphyloma is an ectasia of outer coats of eyeball (cornea, sclera or both) with an incarceration of the uveal tissue.

- *Posterior staphyloma* is due to ectasia of sclera at posterior pole, seen in high myopia
- *Anterior or corneal staphyloma* is d/to ectasia of cornea at anterior pole, seen in corneal ulcer, perforation
- *Ciliary staphyloma* is seen in scleritis, end stage/absolute glaucoma, developmental glaucoma

Corneal tattooing

- *Indicated in*
 1. Leucoma (t/t of choice is keratoplasty but in blind eye with leucoma tattooing is performed for cosmetic purpose)
 2. In traumatic loss of iris (to eliminate monocular diplopia).
 3. Iris coloboma, in large iridectomies
- *Contra-indicated in* adherent leukoma, anterior staphyloma, keratoectasia, neurotropic cornea, phthisis bulbi, glaucoma.
- Gold/platinum chloride with India ink is the m/c method of corneal tattooing.

Keratoplasty

- DSAEK (Descemet's stripping automated endothelial keratoplasty) . Endothelial cell loss is ~34% (more than PKP). Sutures are not required & post-op refractive errors are least.
- PKP (Penetrating keratoplasty) is a conventional method.

Cornea Transplant

- Post op infections :
 - M/c bacterial > fungal
 - Among bacterial : MRSA > Staph epidermidis
 - Among fungal : Candida is most common.
- Penetrating keratoplasty is the m/c method used for it.

D/S OF UVEAL TRACT

- Thinnest part of sclera is --- Lamina cribrosa of optic disc, situated posterior to attachment of m/s.
- Uveitis c/b classified as acute and chronic or granulomatous and non-granulomatous.
- M/c presentation : Sudden onset ocular pain which worse at night + photophobia & lacrimation.
- Characteristics of various uveitis are given below:

Acute Non-granulomatous uveitis

Example	Char/f	Other findings
Behcet's	HLA-B5 association	Posterior uveitis may be +nt
Syphilis	Diffuse chorioretinitis (salt & pepper fundus),	Localised juxta-papillary chorioiditis
UGH syndrome	Uveitis, glaucoma, hyphaema	
VKH syndrome	Uveitis with encephalitis	
Toxoplasmosis	Acute posterior uveitis, Choroiditis + intense vitrieties (head light in fog appearance)	
Psoriatic arthritis	HLA-B ₂₇ association	

Chronic - granulomatous d/s and uveitis

Example	M/c ocular manifestation	Other findings
Sarcoidosis	Candle wax drippings+, Venous sheathing/periphlebitis	Exudates along the walls
TB	Phlyctenular conjunctivitis	Chronic uveitis

- TOC for hypertensive uveitis --- Atropine.

- *KP's (Keratic precipitates)* are diagnostic of anterior uveitis (iridocyclitis). Cells deposit in BM of cornea.
 - Mutton fat KP's are seen in - Ant. uveitis.
- *Koepe nodules* are seen in granulomatous uveitis. on the surface of iris.
- *Bussacca nodules* are seen on the surface of iris.
- *Snow banking* is seen in pars planitis.

D/d of acute conjunctivitis, acute anterior uveitis & acute congestive glaucoma.

Features	Acute conjunctivitis	Acute anterior uveitis	Acute congestive glaucoma
Colored halos	+	-	+
Constitutional symptoms	-	+	++ (Prostration & vomiting)
Loss of Vn	- or mild	+	++
Pain	-	++	+++
Tenderness	-	++	++
Discharge	Mucopurulent	Watery	Watery
Injection (congestion)	Superficial conjunctival	Deep ciliary	Deep ciliary
IOT	N	N	↑
Cornea	N	KP's	Edematous
Iris	N	Muddy	Edematous
AC	N	Deep	Very shallow
Aqueous	N	Flare+	Flare+
Vitreous	N	Hazy	N
Pupil	Pin point Direct light reflex -nt or sluggish	APD, consensual reflex +nt	Oval, dilated, non-reactive

Sympathetic ophthalmia

- Perforating injury in one eye can lead uveitis in other (fellow) eye. Usually follows 2wks to 3 months of injury. Never reported before 2 wks.
- D/to autoimmune reaction to uveal antigen.
- Granulomatous panuveitis.
- First symptom: Difficulty in near vision > photophobia.
- **Retrolental flare** is the first sign.
- Other ocular findings: **Dalen fuch's nodules**.

Atypical Anterior Uveitis

- *Fuch's heterochromic cyclitis* is u/L atypical anterior uveitis(non-granulomatous). A/w stellate/star shaped KP's but no posterior synachie.
- *White uveitis in JRA* eye is not red/congested. Seen in seronegative (RF-ve) pauciarticular uveitis. HLA B27-ve. IOL implantation is contraindicated.
- *Idiopathic uveal effusion syndrome* is a congenital abnormality of sclera/ vortex veins which results in prolonged exudative detachment of uvea, choroid, scleritis. Effusion is seen b/w sclera and choroid. More in hypermetropes.

- All arthritis causing uveitis except JRA are HLA B27 +ve.
- Caterpillar hair in eye can cause nodule in iris, ophthalmia nodosum.
- River blindness is caused by onchocerciasis, which causes non-granulomatous uveitis. DOC is ivermectin.
- TOC for hypertensive uveitis---Atropine.

Choroidal neovascularisation

- Conditions a/w CNV
 - ARMD (m/c)
 - Trauma (choroidal rupture)
 - Angiod streaks
 - Pathological myopia
 - Chorio-retinal scars/dystrophy
 - Intraocular inflammation
- Metamorphosis, macular edema, decreased central Vn.
- Dx: ICG angio/ fluorescein angiography is mainly indicated in choroid pathology.

LENS

- Lens capsule is thinnest at posterior pole.
- Youngest fibres are seen at cortex.
- Lens fibres are formed throughout life.
- Lens derives its nutrition entirely from aqueous humour.
- Aldose reductase pathway (resulting in accumulation of sorbitol) becomes active when there is excess glucose in the lens as in diabetes.
- Ascorbic acid in lens is derived from myoinositol phosphate.

CATARACT: Important Types

Conditions	Type of cataract, Other findings	Location of cataract/
1. Diabetes	Snow flake/ snow-storm cataract	All over cortex
2. Galactosemia	Oil drop	-
3. Chalcosis	Sunflower	-
4. Myotonic dystrophy	Inverted christmas tree/ stellate	Posterior subcapsular
5. Blunt trauma (contusion)	Rosette shaped cataract, Voissious ring at the ant. capsule of lens, Berlin's edema at macula, Commetio retinae	Posterior cortex
6. Rubella	Nuclear, pearly, lamellar cataract	Nuclear
7. Tetany/Hypoparathyroidism	Crystalline flakes opacities	-
8. Lamellar	"Spoke of a wheel" pattern (riders)	Cortical
9. Down's	Multiple flakes/punctate opacities, Bruchfield spots	-
10. Complicated	Polychromatic lustre, Bread crump appearance	Posterior subcapsular
11. Steroids	Use of systemic steroids is a/w cataract	Posterior subcapsular
12. Radiation	-	Posterior subcapsular
13. Atopic dermatitis	Shield cataract	Posterior subcapsular
12. Wilson's d/s	Sunflower cataract, KF rings	Anterior capsular,

- **Complicated cataract**
 - Secondary to inflammation / degeneration (Iridocyclitis, choroiditis, high myopia, RD).
 - Polychromatic luster and rainbow vision is diagnostic.
 - Posterior cortical cataract and spreads in axial length.
 - Bread-crumbs appearance.
- **After cataract**

Posterior capsular opacification (secondary cataract) seen as a complication of ECCE. **Ring of Sommering & Elsching's pearls** are seen. Pupillary block glaucoma may occur because of membrane. Treated by Nd-YAG posterior capsulotomy.
- M/c complication of Morgagnian cataract : Phacolytic glaucoma.
- M/c complication of hypermature nuclear sclerosis : Subluxation of lens.

→ Nuclear cataract can cause → myopia

→ Posterior staphyloma is seen in → pathological myopia.

→ Post- traumatic cataract in a child is treated by → Sx f/b correction of refractive errors with glasses to prevent amblyopia.

Developmental /Newborn Cataract

- T/t is not indicated in developmental cataract unless vision is considerably impaired.
- Unilateral cataract should be operated before 6 weeks and is followed immediately by contact lens fitting.
- Surgical techniques available for removal of cataract are
 - Lens aspiration
 - Lens aspiration with anterior vitrectomy
 - Lensectomy (limbal or pars plana route)

Lenticonus

Anomaly in which post/ant pole of lens assumes a conical shape

- **Anterior lenticonus** --- Ehlers Danlos syndrome, Alport Syndrome
- **Posterior lenticonus** --- More common because lens is thin posteriorly. Occurs as an isolated anomaly or in Alport.

Subluxation of lens, Ectopia lentis

Cong. dislocation of lens

- **Supero-temporal** : In Marfan's syndrome
- **Infero-nasal** : In Homocystinuria
- **Antero-inferiorly** : In Weill-Marchesani syndrome

Contact Lens

- If reticular pattern on the corneal epithelium is seen, it is s/o Acanthamoeba. Found in soft contact lens wearers who wash lens with tap water. Painful condition d/to perineural invasion.
- Thiomersol used as a preservative in contact lens solution. It can cause of allergic conjunctivitis.
- Foldable lenses are made up of acrylic silicon, hydrogen.
- Contact lens in keratoconus : RGP lens.
- Tone lenses - Contact lens with cylindrical correction.
- Hard contact lenses & IOL lens are made up of PMMA (Polymethyl methacrylate)
- Soft contact lenses are made up of HEMA.

Uses of contact lenses

- Anisometropia
- Aphakia U/L
- Astigmatism irregular (Keratoconus, corneal scar)
- High myopia
- Bullous keratopathy

Tinted contact lenses used in-

- Albinism (relieves photophobia)

- M/c infection in contact lens users--- *Pseudomonas*.
- *Pseudomonas* can develop antibiotic resistance by biofilm production in contact lens keratitis.
- Late onset endophthalmitis after IOL is caused by *Propionibacterium acne*.

GLAUCOMA

- POAG has been called the most common "form" of glaucoma.
- Earliest field defects in glaucoma → Central/paracentral scotoma in Bjerrum's area.
- *Secondary glaucoma* is c/by formation of anterior synchia d/to pupillary block, plasmoid aqueous (hypertensive iridocyclitis), → Central/paracentral
- Pupillary block is caused by seclusio pupillary or by IOL lens implantation.
- **Glaucum flecken** are seen in acute angle closure glaucoma.

Investigations for Glaucoma

- *Goldman's tonometer* : Most reliable in measuring IOT.
- *Applanation tonometer* : More reliable than indentation.
- *Tonography* : To measure the facility of aqueous outflow.
- *Campymetry* : Central visual field charting.

Type of Glaucoma	Mechanism, or Due to	Definitive T/t	Medical T/t
POAG (Primary open angle)	Degenerative change in outflow (>20°)	Peripheral iridotomy with NdYAG	Pilocarpine drops
ACG (Narrow angle)	Acute congestive, Narrow ∠ of AC (<20°)	Laser iridotomy	Pilocarpine drops (1st t/t)
Buphthalmos	Defective uveo-sacral outflow		
Absolute		Cyclocryotherapy	
Malignant/Inverse			Atropine
Neovascular	CRVO, DM, Eale's, SCD	PRP with Argon-L	

NARROW ANGLE GLAUCOMA*Stages of Narrow angle glaucoma***1. Prodromal stage:**

Transient attack of ↑ IOT, colored halos, shallow AC

2. Stage of constant instability :

Diurnal variation of ↑ IOT

3. Acute congestive stage :

Sudden neuralgic pain, intense ciliary congestion, vertically dilated non-reacting pupil. A typical attack occurs in one eye in dark environment in emotionally upset pt. Aqueous flare, glaucomatous cupping.

4. Chronic congestive stage :

Cupping of optic nerve head.

5. Absolute glaucoma stage :

Hard, painful & blind eye. Ciliary/equatorial staphyloma may develop.

- *Fincham test* can differentiate b/w halos of glaucoma & immature cataract.

- *Vogt triad* in acute congestive glaucoma: Goniosynchesis + pigment deposition + glaucoma fleeting.

- Sympathetic stimulation can precipitate the attack of ACG so epinephrine and atropine are contraindicated.

T/t of acute congestive glaucoma

- M/m of ACG/ acute angle closure glaucoma is essentially surgical.
- Medical m/m: Emergency and temporary measure to relieve crowding of iris by instillation of **pilocarpine drops**.

Surgical treatment: Definitive

- Peripheral iridectomy* – Indicated when peripheral anterior synechiae are formed in less than 50% of angle of AC and as prophylaxis in the other eye. Laser iridotomy is non-invasive, and is a good alternative to surgical iridectomy
- Filtration surgery for peripheral anterior synechiae >50%, not responding to medical therapy
- Prophylactic treatment in fellow eye* – **Laser or surgical peripheral iridectomy is performed on the fellow asymptomatic eye some days after surgery**

Neovascular Glaucoma

- Characterized by rubeosis iridis
- Causes --- **CRVO (36%), Diabetes (32%), Sickle cell retinopathy, Eale's disease, Chronic RD**
- T/t - Pan retinal photocoagulation with argon laser.

Epidemic Dropsy glaucoma

- Toxic & hypersecretory glaucoma which is non congestive in nature and caused by the toxic action of sanguinarine.
- Sanguinarine causes generalized capillary dilatation and ↑ formation of aqueous → markedly ↑ IOT.
- Coloured halos are seen.
- T/t - Anterior sclerotomy is TOC

T/t of Congenital or infantile Glaucoma

- Medications are not very effective
- The most effective surgery is goniotomy or trabeculotomy
- If all forms of trabeculotomy fail then a trabeculectomy with pharmacological modulation may be considered
- Prognosis is worse if the glaucoma is present since birth and best if it is from 2 months to 1 year of age.

APHAKIA

- Aphakia means absence of crystalline lens from eye
- Eye becomes highly hypermetropic 10-11D
- Power of aphakic eye is 44D.
- All accommodation is lost
- C/f
Deep AC, Jet black pupil, tremulousness of irils, loss of 3rd, 4th Purkinje images (Only 2 purkinje images are seen).
- "Jack in the box" phenomena is seen after ICCE.
- T/t
Image is magnified by 30% in aphakia so spectacles are not useful in unocular aphakia, contact lens suits better
Posterior chamber IOL implantation is TOC

RETINA

- Most radioresistant structure in retina --- Ganglion cell layer.
- Macula lutea has a diameter of 5.5 mm.
- VEGF is thought to be the most important molecule involved in the neovascularization of retina.
- Cholinergic amacrine cells (inner plexiform layer) can secrete Ach & GABA.
- A-waves in ERG are produced by - rods & cones.

DIABETIC RETINOPATHY

- Common in DM type -I.
- Most important factors in development of DR are :
Duration of d/s & **control** of blood sugar.
- Fundus examination is advocated in type I after 5 years, while in type II immediately.

NPDR (Background retinopathy)	<ul style="list-style-type: none"> - M/c form - Earliest sign of NPDR is capillary microaneurysm - Macular edema is m/c cause of ↓ vision (blindness) - Hard exudates, cotton wool spots - Focal argon laser photocoagulation
PDR	<ul style="list-style-type: none"> - Neovascularization of optic nerve is hallmark - RD leads to blindness - vitreous detachment and vitreous hemorrhage - T/t panretinal photocoagulation, vitrectomy

Indications of panretinal photocoagulation (scatter laser)

1. PDR
2. Proliferative retinopathy of Coats

M/m of diabetic retinopathy

1. Background -- Control, follow up
2. Maculopathy, CSME -- Focal retinal photocoagulation
3. Diffuse leaks around macula/ Circinate maculopathy -- Focal retinal photocoagulation
4. Pre proliferative stage -- Frequent review
5. Proliferative (PDR) -- Panretinal photocoagulation
6. Advanced disease -- Vitreo-retinal surgery

Important Eye Findings in DM

- Snow flake (snow storm) cataract:
Snow flakes opacities develop all over the cortex giving a milky white colour to the lens. There is accumulation of sorbitol and fructose in lens.
- In advance stage :Tractional RD, senile cataract, neovascular glaucoma etc.

HYPERTENSIVE RETINOPATHY

- Always b/L.
- Patient with systemic HTN has frequent headaches.
- Vasoconstriction of the retinal arterioles is primary response to the raised BP.

Grading (Keith-Wagener-Barker classification)

Grade I --- Consists of mild arterial attenuation, broadening of the arteriolar light reflex.

Grade II --- Marked generalized narrowing and focal attenuation of arterioles associated with deflection of veins at arteriovenous crossings (Salu's sign)

Grade III --- Grade II + Copper wiring of arterioles flame shaped hemorrhages, cotton wool spots, hard exudates.

Banking of veins distal to AV crossing---

Bonnet's sign

Tapering of veins on either side ---Gunn's sign

Grade IV --- Grade III + Silver wiring + *papilloedema*.

Central retinal artery occlusion (CRAO)

- There is sudden painless loss of vision.
- Signs** -- Direct papillary reflex is absent (afferent pupillary defect). Arteries are narrowed. Retina is milky white due to oedema. In central part of macula **cherry red spot** is seen. "**Cattle track**" appearance seen on fundoscopy which is characteristic of branched RAO.

Retinal Dystrophies

- Dystrophy is idiopathic spontaneous change with no inflammatory component.
- Best d/s:** Dystrophy of ocular layer of retinal pigment epithelium.
- Stargardt's d/s:** Dystrophy mainly limited to macular region.

Retinal degeneration

- Peripheral retinal degeneration (Lattice & Snail track type) is found in --- Myopia, Marfan's, EDS, Stickler's syndrome
- Require prophylactic t/t to prevent dvpt of RD (retinal detachment)

→ *Purtscher's retinopathy is a traumatic retinal angiopathy m/c seen after head/chest trauma (d/to occlusion of posterior retinal artery). Also seen in acute pancreatitis, SLE, after child birth*

→ *Retinal detachment is best detected by--- Indirect ophthalmoscopy*

→ *ETDRS (Early Treatment for Diabetic Retinopathy Scale) is used for early detection of vision in DR patients*

RETINAL DETACHMENT (RD)

- Separation of neurosensory retina proper from pigment epithelium.
- Types of RD:

Primary / Rhegmatogenous RD	Exudative RD	Tractional RD
Cause A/w retinal breaks • Myopia • Aphakia • Lattice retinal degeneration • Trauma	• Neoplasm i.e. malignant melanoma of choroid, retinoblastoma • Infection • Vascular lesion - CSR, exudative retinopathy	D/ to vitreoretinal traction bands • Post traumatic • PDR • ROP • Sick cell retinopathy • Proliferative retinopathy of Coats
C/I		
• Dark spots (muscae volitantes) or floaters in front of eye • Photopsia (sensation of flashes of light) • Sudden painless loss of vision • Retinal tears/breaks in upper temporal quadrant	• No photopsia, tears, folds, undulation seen • Shifting fluid with gravity is hallmark • Opaque	• Presence of vitreoretinal bands • No tears seen
T/t		
• Sealing of retinal breaks • Scleral buckling/ encircage	• Spontaneous regression, Enucleation if neoplasm+	• Pars plana vitrectomy and internal tamponade

- In RD, anterior segment examination by slit-lamp reveals fine pigmented cells/tobacco dust on the anterior face of the vitreous k/as *Shaffer's sign*. With no h/o trauma/Sx it is pathognomonic of a retinal break.
- A recent onset RD ↓ es IOT while long-standing RD ↑ es IOT.

Eales D/s

- Periphlebitis retinae
- Seen in young males
- D/to allergy to tubercular Ag.
- Presents with recurrent vitreous h'age.

Angiod Streaks

- Breach in Bruch's membrane.
- Seen in pseudoxanthoma elasticum, EDS, SCD, thalassemia, Paget's d/s.

Bulls eye maculopathy

- Circular bundles of different shades of pink/orange are visible.
- Seen in progressive cone dystrophy, Stargdt's d/s, Batler d/s, hydroxy chloroquine toxicity.

Central Serous Retinopathy (CSR)

- Self limiting d/s of young males
- Fluorescein pattern : Smoke sack/enlarging ink pattern

Cystoid macular Edema (CME)

- FFA/Fundoscopy : "Flower petal pattern"

Important Retinal findings

- *Cotton wool spots (cytoid bodies)* are d/to focal ischemia in the **nerve fibre layer**. Found in HIV retinopathy. Acute branch retinal vein occlusion, CRVO
- *Flame shaped (or striate) hemorrhages* in retina are d/to superficial hemorrhage in the nerve fibre layer of retina and seen in *hypertensive and arteriosclerotic retinopathy*.
- *Macular star* is d/to accumulation of transudate in Henle's layer and is seen in papilledema and Hypertensive retinopathy grade IV.
- *Macular scar* is found in healed chorioretinitis.
- *Neovascularization* of retina is seen in proliferative diabetic retinopathy (hallmark of PDR), sickle cell disease (sea-fan neovascularization).

Finding	Site of tear	Location
Retinal tear	PCL & RPE	Superotemporal
Macular tear	Full thickness tear	Inferotemporal

Retinitis Pigmentosa (RP)

- Slow degenerative disease / dystrophy of photoreceptors of retina (**rods** > cones).
- Usually involves both eyes
- Usually **AR** inheritance
- M/c symptom is nyctalopia (night blindness)
- *Cliff*: Triad of
Pale waxy disc + Attenuated/narrowed arteries + Bony spicules/ Bone corpuscle formation.
- Visual field changes –
First change in perimetry **annular or ring scotoma**, later → **tubular vision**
- ERG is abnormal (amplitude ↓).

- M/c systemic association : Usher's syndrome (deafness)
- Also a/w LMB syndrome, **NARP** syndrome (Neuropathy + Ataxia + RP), **abetalipoproteinemia** (Bassen Kornzweig d/s), Cockayne's, **Refsum's** d/s, Hallgren's syndrome, , Kearns's Sayre syndrome, Refsum's d/s, etc.

- *Tubular vision is also seen in quinine toxicity.*
- *ETDRS (Early Treatment for Diabetic Retinopathy Scale) is used for early detection of vision in DR patients*
- *HIV retinopathy is c/by --- Cytoid bodies*

Causes of Night blindness (Nyctalopia)

- Vit **A** deficiency
- **RP**
- High/pathological **Myopia** (> 6D)
- Peripheral cortical cataract
- Sorsby's fundus dystrophy
- Oguchi disease
- Refractive surgery (RK, PRK, LASIK)
- Rarely in late stage of 1° open angle Glaucoma.

Causes of Day blindness (Hemeralopia)

- Central corneal opacity
- Central lenticular opacity
- Congenital absence of cones [3'c]

OPTIC NERVE

- Length of optic nerve is : 3.5 to 5.5 cm
- Longest part of optic nerve is intra-orbital (2.5 -3 cm).
- First sign of optic nerve d/s: APD (afferent pupillary defect).

Optic Neuritis

- *Pathognomic features of retrobulbar neuritis:-*
 1. Pain on elevation of eye. It is becoz some of the fibres of SR m/s are attached to optic nerve myelin sheath.
 2. RAPD (Marcus Gunn pupil).
- Field defect in optic neuritis: central scotoma
- *Ischemic optic neuritis:-*
 1. Arterial.
 2. Non-arterial: altitudinal field defects.
- Most prominent symptom of optic neuritis - Sudden loss of Vn.

Features	Optic neuritis	Papilloedema
Usually affects	u/L	b/L
Onset	Sudden	Insidious/chronic
Loss of Vn	Marked	Negligible, Gradual
Tenderness	+ (At the insertion of MR & SR)	-
Other symptoms	-	Headache, N, V
Swelling (Edema) of the disc	2-3 D	>3D (Marked)
Visual field defect	Central, centrocecal scotoma	Enlargement of blind spot
Posterior vitreous	Fine opacities	Clear
Fluorescein angio	Pulling of dye around vessels	H'age & exudates are seen (cottonwool spots)
Pupil	Pin point Direct light reflex -nt or sluggish	APD, consensual reflex +nt

Toxic Amblyopia

- Field defect in TA: centro-cecal scotoma
- Amaurosis: Total loss of vision.
- Amblyopia: Partial loss of vision.
- Amaurosis fugax: Transient loss of vision in a certain mannner (first superior → middle → then inferior).

ON Glioma

- ON glioma is an **astrocytoma**.
- Common in **NF-1**.
- Proptosis, Amblyopia: Partial loss of vision.
- Seen in children

- Optic sheath meningioma is a/w V_n loss + proptosis in middle aged females.
- Optic disc angioma is a/w **VHL syndrome** in 3-4th decade.
- Optic nerve lesions are a/w absent direct & consensual +nt.
- Vitamin B12 deficiency can produce centrocecal scotoma.

Imp. Mitochondrial Disorders

- Leber's hereditary optic neuropathy (LHON):-**
 - D/to mutation at maternal mitochondrial gene.
 - Atypical as pupillary reaction is normal.
- Chronic progressive external ophthalmoplegia (CPEO):-**
 - Mitochondrial disorder.
 - Ptoxis without diplopia.

Kearn's Sayre Syndrome (KSS):-

Multi-organ mitochondrial d/s with onset <20yr c/by a triad of:

- CPEO
- Pigmentary retinopathy
- +
 - Any 1 of these → Cardiac conduction defects, CSF protein >1 g/L, cerebellar ataxia.

STRABISMUS/ SQUINT

Type	Sub-type	C/E or e.g.	T/t
Concomitant (Non-paralytic)	<i>Heterophoria (Latent squint)</i>		Orthoptic exercises
PD = SD	<i>Heterotropia (manifest squint)</i>		Orthoptic exercises
Paralytic Squint	<i>Esotropia (Convergent)</i>	Uncrossed/ homonymous diplopia	Surgery
SD > PD (2° deviation >1°)	One or both eyes turn inward d/to LR palsy		
	<i>Exotropia</i>	Crossed/ Heteronymous diplopia in rt 3rd nerve palsy	Surgery

[Remember Crossed in exotropia]

Convergent squint or Esotropia or esodeviation

- Denotes inward deviation of one or both eye. The angle of deviation is fairly large
- Infantile esotropia develops within 6 months of life with no limitation of ocular movements and there is **no significant refractive error**.
- Fixation is alternating. The child uses his right eye in left gaze and vice versa.
- Horizontal nystagmus is seen
- Inferior oblique m/s overactivity is seen to compensate the squint

T/t of Amblyopia

- Amblyopia should be treated as soon as possible. The best time to correct amblyopia is infancy or early childhood. After the 9 yrs of age visual system is

fully developed and can't be changed.

- To correct amblyopia **patching of the good eye** (Occlusion of normal eye) is advocated for weeks-months. The children who can't tolerate a patch can sometimes be treated with atropine therapy called **penalization**. (Tropicamide is fastest acting least cycloplegic. Atropine is maximum cycloplegic, longer acting and deeper acting.)

T/t of Squint

- TOC for paralytic squint --- Surgery
- TOC for amblyopia with unilateral strabismus --- Conventional occlusion (of normal eye)
- TOC for accommodative squint --- Correction of refractive errors (eye glasses and contact lenses)
- TOC for concomitant squint --- Orthoptic exercises

INJURY TO EYE BALL

Intraocular Foreign Bodies

- *Chisel & Hammer* – Chips of iron and steel
 - Mc intraocular FB (90%)
- *Copper* **Chalcosis**
 - KF rings (in Descemet's membrane)
 - Sunflower cataract
- *Iron / Steel* **Siderosis bulbi**
 - Ant. epithelium & lens capsule involved
 - Pigmentary changes in retina, V_n loss, mydriasis, sec. glaucoma

→ FB can be detected by slit lamp + gonioscopy

→ Berman's locator is helpful in differentiating magnetic FB from non-magnetic FB

Photophthalmia & Photoretinitis

	Photophthalmia	Photoretinitis
1. Also k/as	Snow blindness	Eclipse burn
2. Cause/ Eye injury by	UV- rays	IR- rays
3. C/F	Corneal epithelial erosions	Macular burn → scar
4. T/t	Pad & bandage	Smoked lenses should be used for protection

ENDOPHTHALMITIS

- **Periphlebitis** is the earliest sign.
- An inflammation of the internal coats of the eye. It is a possible complication of all intraocular surgeries, particularly cataract surgery > cornea transplantation and glaucoma filtering.
- Exogenous endophthalmitis is the m/c form and occurs after penetration of the eyeball from trauma, surgery or erosion of an external eye infection into the eye.
- Endogenous endophthalmitis seen in immunocompromised individuals.

D/S OF ORBIT

- Shape of the orbit is --- Quadrilateral/pyramidal.
- Capacity of the orbit is --- 30 cc
- Orbit volume is --- 30 ml
- Eye volume is --- 6.5 ml
- Walls of orbit
 - Posteromedial wall : M/c site of blowout # of floor (Situated just medial to infraorbital neurovascular bundle)
 - Medial wall : Weakest wall of orbit (Formed by cribriform plate of ethmoid bone)
- *Reid base line* passes through the lowest part of the infraorbital margin and the middle of the external auditory meatus.
- *Bare orbit sign* is seen in sphenoid wing dysplasia.

PROPTOSIS (Exophthalmos)

- Clinically significant proptosis is defined as a minimum difference of ≥ 2 mm as measured by exophthalmometer
- Hertel mirror exophthalmometers are used to measure the degree of protrusion of the eyeball
- The mnemonic VEIN is helpful in remembering the causes of proptosis.
 - V - Vascular causes
 - E - Endocrine causes
 - I - Inflammation and infective causes
 - N - Neoplastic causes
- Carotid cavernous fistula (high flow shunts) may arise as a result of trauma or spontaneously. These patients have subjective bruits, proptosis, chemosis and vision loss.
- Causes of pulsatile proptosis :
 1. Carotico-cavernous fistula
 2. NF-1
 3. # Roof of orbit

Unilateral	Bilateral
Rhabdomyosarcoma	ALL,
Orbital cellulitis, orbital tumours/cyst	Endocrine: Thyrotoxicosis
Early stages of cavernous sinus thrombosis	Late stages of CST
Orbital varix	Apert's/Crouzon's

- Cavernous hemangioma is m/c benign intraconal tumour in adults. Seen in 2nd-4th decade. Presents with slowly progressive painless proptosis.
- Capillary hemangioma occurs in infants 6-10 months. mostly extraconal. have an arterial supply from either the ECA or ICA.
- **M/c** cause of intermittent proptosis : Orbital varix (varicose vein in the eye).

PTOSIS

- M/s involved : LPS & Muller's.
- LPS palsy is a/w pseudo-enophthalmos (ipsi/L ptosis + contr/L proptosis).
- Paralysis of Muller's m/s or orbitalis m/s is a/w-enophthalmos with ptosis. Orbitalis m/s palsy c/b seen in Horner's syndrome.
- Blepharophimosis is a congenital syndrome of ptosis

Classification:

Group	Classes	Examples
Myogenic	Congenital	Blepharophimosis syndrome (ptosis + ectropion of lower lid + telecanthus/ epicanthus inversus)
	Acquired	MG
Neurogenic	3rd CN palsy	
	Horner's	
Aponeurotic	D/t to dehiscence of aponeurotica	Post op, Old age
Mechanical	Conjunctival scarring	Trachoma, burns, SJS
	Other causes	Chalazion, tumours

EYE TUMOURS

In children

- **M/c** intraocular tumour --- Retinoblastoma
- **M/c** intra-orbital tumour --- Rhabdomyosarcoma

In adults

- **M/c** intraocular tumour --- Malignant melanoma choroid
- **M/c** intra-orbital tumour --- cavernous hemangioma
- **M/c** tumour which metastasize to eye - Neuroblastoma
- **M/c** tumour of eyelids --- BCC
- **M/c** tumour of lacrimal gland - Benign mixed tumour.

Retinoblastoma

- **M/c** age of presentation in RB : 18 months
- **M/c** presentation in RB : Leucocoria (strabismus is 2nd m/c).
- Mutations in RB are seen at 13q14.
- Optic foramen is enlarged.
- Calcification is common (Intra ocular/cranial).
- Laser or cryo are done when tumour size is <3mm.
- Trilateral RB is B/L RB + pineal gland tumour
- IOP is ↑ed in RB while IOP is normal in pseudoglioma.
↑ed LDH, phosphogluco-isomerase & NSE are found in RB.
- **M/c** non-ocular malignancy in RB → Osteogenic sarcoma.

Pseudoglioma

- Seen in
 - Tuberculoma of choroid
 - Plastic iridocyclitis
 - Toxocara choroiditis
 - RD, Retrolental fibroplasia
- IOT is normal.
- LDH is normal or ↓ed in vitreous humour.

Choroidal melanoma

- **M/c** intraocular tumour in adult.
- Poorest prognosis is of epitheloid cell type.
- Best prognosis is of spindle type A.

POSTERIOR CHAMBER

Vitreous opacities (Floaters)

- K/as Floaters.
- Can be:

- Inflammatory, hemorrhagic, pigment cells
- *Synchiasis scintillans* : Composed of cholesterol bodies.
- *Asteroid bodies* : Composed of calcium + lipids.
- *Muscae volitantes* : Very small sized remnants of hyaloid vessel.
- Vitreous is composed of **type II** collagen + hyaluronic acid.

Remnants of Hyaloid vessel

- Very small : *Muscae volitantes*
- Intermediate sized :
Mittendorf dots (at the back of lens),
Bergmister papilla (at optic disc)
- Very large sized : PHPV (Persistence of vessel). PHPV arc a/w trisomy 13 and trisomy 22.

EYE LIDS

	Harderianum externum (Strye)	Harderianum internum	Chalazion (Tarsal cyst)
Inflama ⁿ of	Acute inflamma ⁿ of - Hair follicles (m/c) - Glands of Zeis - Glands of Moll	Acute inflamma ⁿ of Meibomian glands	Chronic lipogranulomatous inflamma ⁿ of Meibomian glands
D/to or k/as	Staphylococcus	-	Tarsal/Meibomian cyst
Pain	++	+	- (painless)

- If chalazion is recurrent suspect mild refractive error or sebaceous cell adenocarcinoma.
- **Telecanthus** is a soft tissue problem in which inter-pupillary distance is normal.
- **Hypertelorism** is a bony problem in which inter-pupillary distance is ↑ed. Seen in variety of syndromes like-DiGeorge, Loeys-Dietz, Apert, Noonan's, LEOPARD, Crouzon's, Wolf-Hirschhorn's, Andersen-Tawil's Waardenburg Cri du chat, Morquio, Hurler's syndrome. also seen in NF and craniofrontonasal dysplasia.
- **Distichiasis** is extra row of eye lashes.
- **Trichiasis** is misdirected eye lashes. M/c after chronic blepharitis (inflammation of lid margin).

- **Madarosis** is loss of eye lashes/ eyebrows (e.g. in leprosy, myxoedema)
- **Foliosis** is Whitening/greying of eyelashes.
- **Tylosis** is thickening of the lid margin.
- **Blepharitis** is inflammation of the eyelid . It is a/w acne rosacea or seborrheic dermatitis.
- **Symblepharon** is adhesion of both bulbar & palpebral conjunctiva. It results either from d/s (conjunctival sequelae of Trachoma) or trauma. Cicatricial pemphigoid and, in severe cases, rosacea may cause symblepharon.

OPHTHALMIC DRUGS

- **VOCLOSPORINE** : is a novel **calcineurin inhibitor** and immunomodulator drug. New agent for the prophylaxis and t/t of non-infectious uveitis, being used in LUMINATE trials. Steroid sparing effect+.

Mydriatics

Drug	Onset of effect	Duration of effect	Remark
Tropicamide	40 min	3-6 hr	Shortest acting (Quickest, briefest)
Phenylephrine	20 min	6 hr	Mydriasis without Cycloplegia
Cyclopentolate	60 min	1 day	
Homatropine	60 min	3 days	Used in elderly/ hypermetropes
Atropine (1%)	40 min	10 days	Most potent, longest acting. Ointment (1%) used in children

- All are mydriatic and cycloplegics except phenylephrine
- Mydriatic used in children --- Atropine ointment as their power of accommodation is high.
- Fastest acting mydriatic and cycloplegic --- Tropicamide
- Shortest acting mydriatic without cycloplegia --- Phenylephrine
- Shortest acting mydriatic and cycloplegic --- Tropicamide

Steroids are useful in

1. Deep/stromal Disciform keratitis
2. Anterior uveitis
3. Phlyctenular conjunctivitis
4. Interstitial, Rosacea/VZV keratitis (in late stages)
5. Episcleritis, scleritis

[but NOT USED in superficial keratitis]

Drugs in t/t of

	Iridocyclitis	Corneal Ulcer	Open angle glaucoma	Closed angle glaucoma
C/nd	Pilocarpine	Steroid	Atropine & steroid	Atropine & steroid
Preferred	Atropine steroids	viral-acyclovir fungal-nystatin, amb	Timolol Argon laser Trabe-culoplasty	Pilocarpine Laser iridotomy

- Atropine & homatropine may precipitate --- Glaucoma in susceptible individuals
- Topical corticosteroids are indicated in T/t of --- Anterior uveitis
- Systemic corticosteroids are indicated in T/t of --- posterior uveitis
- C/c of prolonged t/t with topical steroids (chronic steroid drops) --- Glaucoma
- C/c of prolonged t/t with systemic steroids --- Cataract

LASER IN OPHTHALMOLOGY

Lasers in Ophthalmology

Argon Laser	---	It absorbs Hb & ↓ hemorrhage Used for PDR, neovascular glaucoma, capillary hemangioma
Nd:YAG Laser	---	For posterior capsulotomy, iridectomies, iridotomies, cutting vitreous bands (vitrealysis), secondary glaucoma after cataract, tumours.
Diode Laser	---	Retinal photocoagulation, For glaucoma drainage
Argon Laser	---	RD, retinal vein occlusion, Eale's ds
Excimer (UV laser)	---	In refractive surgery LASIK (For T/t of myopia, astigmatism, hypermetropia) also used for photorefractive keratectomy (in Band Keratoplasty)

- Lasers used for retinal photocoagulation are --- Diode laser, krypton red laser, double frequency Nd:YAG
- CO₂ Laser is used for intracellular boiling (skin cancer)
- Holmium laser acts by coagulation effect in BPH, can be used for lithotripsy & all type of stones

BLINDNESS

Colour blindness

- Red-Green CB = X-Recessive
- Blue CB = A-Recessive
- Mc congenital CB = Green (Deuteranopes), blue rare.
- Mc acquired CB = Blue (deuteronopia)

- In Digitalis toxicity - Yellow vision (Xanthopsia)
- In Ethambutol toxicity vision is Red (Red remains green goes).
- Erythropsia (red Vn) - after cataract surgery, in snow blindness
- Blue Vn is seen in -nuclear cataract, digitalis toxicity

M/c cause of Blindness/loss of vision in

- In AIDS patients --- CMV retinitis
- In Malaria --- Optic neuritis
- In elderly --- Macular degeneration
- In DM
Proliferative type --- RD
In NPDR --- Macular edema
- In pregnancy --- Toxemia of pregnancy → CRAO

WHO Blindness Criteria

Visual impairment	Best corrected visual acuity in better eye	WHO grade & NPCB criteria
0 (Normal)	6/6 to 6/18	N
1 (Visual impairment)	< 6/6 - < 6/18	Low Vision
2 (Severe Vn impairment)	< 6/60 - 3/60	Economic blindness (Work Vn)
	3/60 - 1/60	Blindness - Social blindness - Work Vn
	1/60	Manifest blindness
	1/60 or less	Absolute blindness

[Mnemonic : LESMA]

- Legal blindness is best corrected VA of < 3/60 in better eye or visual field of < 10°. (also k/as travel vision, patient is unable to count finger at 3 meter).
- Economic blindness is best corrected VA of < 6/60 in better eye.
NPCB, India defines blindness as VA < 6/60 in the better eye with the available correction (also k/as work Vn.)
- Refer to ophthalmologist when VA is 6/9.
- Prevalance of blindness = 0.56%
- Prevalance of blindness in > 50 yr = 1.1 %

- Incidence of cataract in blinds = 62.6 %

Major Causes of blindness in India

Eye Defect	ICMR (1971-74)%	NPCB (1986-89)%
Cataract	55	80.1
Refractive Errors	NA	7.35
Aphakic Blind	NA	4.69
Trachoma	5.0	0.39
Vitamin A Deficiency	2.0	0.02

- M/c cause of blindness worldwide → cataract
[Cataract > refractive errors > aphakic blindness]
- M/c cause of blindness in India is **cataract**
[Cataract > refractive errors > aphakic blindness]
- M/c cause of ocular morbidity → Refractive errors
- M/c cause of ocular morbidity in youngs → Refractive errors.
- M/c cause of preventable blindness in children → vitamin A deficiency.
- M/c cause of irreversible blindness worldwide (or in children) → Glaucoma
- State with maximum number of blind --- MP
- SAFE strategy is recommended for the control of --- Trachoma
- Screening strategy for the control of blindness under NPCB --- High risk screening

Cortical blindness

- D/to bilateral infarction in the distal portion of cerebral arteries.
- Pupillary reactions are preserved.
- Pt is unaware of blindness & may deny it (Anton's syndrome)
- Tiny islands of vision persist.

Vision 2020

- WHO programme includes 5 diseases :
Cataract, Trachoma, Onchocerciasis, Childhood blindness, and Refractive errors.
- Indian programme includes :
Cataract, Trachoma, Diabetic retinopathy, Glaucoma, and corneal blindness, Childhood blindness, and Refractive errors. [Excludes onchocerciasis]

Common causes of sudden painful loss of vision

- Acute congestive glaucoma
- Acute iridocyclitis
- Chemical and mechanical trauma to eyeball

Common causes of sudden painless loss of vision

- Macular edema, macular degeneration
- Eale's d/s (vitreous and retinal hemorrhage): Young
- Rhegmatogenous or primary RD : In elderly
- CRAO, CRVO
- Optic neuritis
- Methyl alcohol amblyopia

LACRIMAL APPARATUS

- Tear production starts at 6 months.
- Tear film has 3 layers
 1. Lipid (secreted by meibomian & Zeis glands)
 2. Aqueous (secreted by lacrimal glands)
 3. Mucous (secreted by goblet glands): Innermost layer
- Sjogrens syndrome (KCS) is d/to aqueous deficiency.
- Opening of DCR is made in middle meatus.
- Mumps causes dacrocystoadenitis.

Congenital Dacrocystitis

- It follows stasis of secretions in the lacrimal sac d/to congenital blockage in the nasolacrimal duct (NLD). Imperforate hasner's valve is m/c cause.
- Epiphora alone should be treated conservatively with local massage.
- Massage is done in direction toward the nasal cavity downwards and medially with a clean thumb & index finger behind the lacrimal crest.

OCULAR MANIFESTATIONS OF DISEASES

- M/c ocular manifestation of measles → Vit A deficiency.
- Mumps causes dacrocystoadenitis.
- Membranous conjunctivitis is seen in Diphtheria.

POINT OF SPECIAL MENTION

- Corneal nerve is visible in - Leprosy, Keratoconus
- Thinnest part of sclera is --- Behind insertion of rectus m/s

while sclera is thickest at posterior pole.

- Aniridia is a/w Wilm's tumour (nephroblastoma)
- **Juxta foveal retinal telangiectasia** is macular vascular abnormality which may be congenital or acquired. It is a condition c/by exudation or diffusion abnormalities of retinal capillaries in juxta foveal region. It may be a/w DM, UC, multiple myeloma, CLL etc.
- **Marcus gunn jaw winking phenomena/ Syndrome** is a congenital abnormality seen in 5% cases of ptosis. It manifests as unilateral jaw winking (retraction of upper eyelid during contraction of pterygoid or during chewing movements.) Levator disinsertion is required + frontalis sling surgery is done to avoid this phenomena.
- **Boxcar segmentation** is seen in both arteries and veins. It is a sign of severe obstruction in CRAO.
- **Mizuo phenomenon** is seen in Oguchi d/s., a rare AR disorder with congenital stationary night blindness.
- Hard exudates seen mainly in DM (in other conditions e.g. HTN soft exudates are common)
- Blue discoloration of sclera ----- In osteitis deformans
Pigmentation of sclera ----- In Melanosis bulbi
- **Ring scotoma** is seen in ----- RP, chronic simple glaucoma, cataract.
- **Dendritic / geographical ulcer** are seen in --- Herpes, vaccinia
- **Herpes Zoster ophthalmicus** is caused by --- Varicella
- **Amaurotic cat's eye** is seen in --- Cyclitic membrane, Cataract, Retrolental fibroplasia
- Proliferative / neovascular retinopathy is the m/c cause of spontaneous vitreous hemorrhage
In DM sudden loss in Vn is due to vitreous hemorrhage
- In Ethambutol toxicity Red remains Green goes. (Red vision persists & loss of ability to see green).
- M/c cause of sudden U/L loss of vision ----- optic neuritis
- M/c cause of an enlarged blind spot (scotoma) ----- raised ICT
- M/c cause of cortical blindness ----- B/L damage to visual radiation or occipital lobe
(for e.g. basilar artery insufficiency, hypertensive encephalopathy)
M/c cause of permanent visual loss in elderly ----- macular degeneration
- M/c cause of CRVO ----- hypercoagulable state
M/c T/t modality for acute angle glaucoma ----- laser iridectomy
- M/c T/t modality for RD ----- laser photocoagulation
- M/c cause of intermittent diplopia that occurs later in the

day ----- myasthenia gravis

- M/c cause of progressive diplopia ----- compressive lesion (e.g. tumour)
- M/c cause of sudden diplopia ----- vascular lesion / infarction
- M/c cause of Argyll Robertson pupil ----- syphilis, DM
- Loss of lacrimation is d/to injury to greater petrosal nerve.

SOME IMP. NEGATIVE POINTS

- Coloured halos are NOT seen in ----- Steroid induced glaucoma, Open angle glaucoma, Tetracycline toxicity, Corneal opacity
- Epiphora (watering from eyes) is NOT seen in an infant ----- in corneal dystrophy
- Follicles over conjunctiva are NOT seen in ----- Spring catarrh, d/to use of soft contact lens
- Papilledema is NOT characterized by ----- Loss of vision, afferent pupillary defect
[In Papilledema there may be transient blurring of vision but vision is never lost (which is often seen in papillitis)]
- NOT a feature of hypertensive retinopathy ----- Arteriolar dilatation, CSR
- Cautery is NOT used for ----- Corneal abrasion with Hypopyon
- NOT seen in oculomotor palsy ----- Convergent squint & Miosis
- NOT commonly seen in herpes zoster ophthalmicus ----- Sclero-keratitis
- Steroids are NOT indicated in ----- Fungal corneal ulcer, superficial keratitis
- NOT a macular function test ----- Retinal ERG
- Indirect ophthalmoscopy is NOT useful in ----- Examination of fovea.
- Retinitis pigmentosa is NOT a feature of --- Hallervorden-Spatz d/s.
- Steroids are NOT indicated in ----- Fungal corneal ulcer, superficial keratitis
- Cricket ball injury to eye does NOT lead to --- Hypopyon
- NOT done in advanced PDR --- Removal of epiretinal membranes
- Cricket ball injury to eye does NOT lead to --- Hypopyon
- Endophthalmitis does NOT involve --- Sclera
- NOT true of corneal transplantation --- Full eye globe is preserved in culture media.

- WHO vision 2020 do NOT include ---- Epidemic conjunctivitis.
- NOT a common cause of childhood blindness ---- Congenital dacryocystitis.

CLINICAL VIGNETTES

- A 25 year old male with BP 120/70 mmHg was found to have IOT of 27 mm Hg. His eyes are normal looking, anterior chamber is clear and angles are open on gonioscopy. No visual field change observed. Diagnosis is--

- A. Open angle glaucoma
- B. Normotensive glaucoma
- C. Ocular hypertension
- D. Angle closure glaucoma

[Ans.: C. Ocular hypertension]

In ocular hypertension --- IOT is mildly elevated but no visual field changes are seen

In normotensive glaucoma --- IOT is mildly elevated but early visual field changes are seen

- A patient comes to eye OPD with complaint of redness of eye. O/E he has hazy cornea, and shallow anterior chamber in fellow eye. Most likely diagnosis is

- A. Acute anterior uveitis
- B. Acute congestive glaucoma
- C. Viral keratitis
- D. Angle closure glaucoma

[Ans.: A. Acute anterior uveitis]

Diagnostic clues are

Acute anterior uveitis --- Red eye, miotic pupil, deep AC (AC of fellow eye is likely to be mistaken as shallow), hazy cornea d/to KPs

Acute congestive glaucoma --- Red eye, oval mydriatic pupil, shallow AC (AC of fellow eye is likely to be mistaken as deep), hazy cornea d/to corneal edema

- A 4 year old boy presents with large cornea, lacrimation and photophobia. D/g is

- A. Megalocornea
- B. Congenital glaucoma
- C. Congenital cataract
- D. Dacrocystorhinitis

[Ans.: C. Congenital glaucoma]

Congenital glaucoma usually appears b/w birth to 5 yrs. It is a/w photophobia & lacrimation. Cornea is large and hazy (blue bull eye)

Megalocornea is c/by large cornea,

- A 20 year old man complaints of difficulty in reading the newspaper with his right eye, three weeks after sustaining a gunshot injury to his right left eye. The most likely d/g is [AIPGMEE 2003]

- A. Macular edema
- B. Sympathetic ophthalmia
- C. Optic nerve avulsion
- D. Delayed vitreous hemorrhage

[Ans.: B. Sympathetic ophthalmia]

Sympathetic ophthalmia refers to panuveitis of opposite eye following penetrating trauma to the primary eye or exciting eye

- A 55 year old patient complains of decreased distance vision. However, now he does not require his glasses for near work. The most likely cause is: [AIIMS Nov'05]

- A. Posterior subcapsular cataract.
- B. Zonular cataract.
- C. Nuclear sclerosis.
- D. Anterior subcapsular cataract.

[Ans.: C. Nuclear sclerosis.]

In patient with nuclear sclerosis, distant vision deteriorates due to progressive index myopia. Such patients are able to read without presbyopic glasses. This improvement in near vision is referred to as 'second sight'.

- A 55 year old female comes to the eye casualty with history of severe eye pain, redness and diminution of vision. On/e the visual acuity is 6/60, there is circumcorneal congestion, corneal edema and a shallow anterior chamber. Which of the following is the best drug of choice? [AIIMS Nov'05]

- A. Atropine ointment.
- B. I.V. Mannitol.
- C. Ciprofloxacin eye drops.
- D. Betamethasone eye drops.

(Ans. B. I.V. Mannitol.)

Clinical picture described in question is suggestive of Acute congestive glaucoma which occurs in course of primary angle closure glaucoma (PACG)

Systemic hyperosmotic agents should be given initially to ↓ IOP I.V. mannitol 1 gm/kg, urea, oral glycerol.

- A 30 year old patient with history of recurrent headache was sent for fundus evaluation. He was found to be having generalized arterial attenuation with multiple cotton wool

spots and flame shaped hemorrhages in both eyes. The most likely cause is: [AIIMS Nov'05]

- A. Diabetic retinopathy.
- B. Hypertensive retinopathy.
- C. Central retinal artery occlusion.
- D. Temporal arteritis.

(Ans. B. Hypertensive retinopathy)

Patient with systemic hypertension has frequent headaches.

- A 25 yr old female presented with sudden, severe loss of vision in both eyes, more so on the right side with no perception of light. On examination she has normal pupillary responses. Optokinetic nystagmus & fundus are normal. She was able to touch tips of her finger with right eye closed but not with the left eye closed. The most likely d/g is:

[AIIMS Nov'11]

- A. Optic neuritis
- B. Anterior ischemic optic neuropathy
- C. Functional visual loss
- D. CMV retinitis.

(Ans. C. Functional visual loss)

Optic neuritis and optic neuropathy both are a/w pupillary defects (RAPD) and fundus changes. Similarly in CMV retinitis there is "crumbled cheese and ketchup" appearance of fundus. So, the d/g of exclusion is ans C.

- A young male presents with blurring of vision in right eye followed by similar symptoms in his left eye 3 months later. On/e his pupillary reflexes are normal but centrocecal scotoma is seen. He has parafoveal telangiectasia and disc hyperemia. Most likely d/g is

[AIIMSMay'2009]

- A. Toxic amblyopia
- B. Papilloedema
- C. Optic Neuritis.
- D. Hereditary optic atrophy

(Ans. D. Hereditary optic atrophy)

- Diplopia with limitation of adduction of right eye with adduction saccades of left eye is seen with normal convergence. It is d/to

[AIIMSMay'2009]

- A. Partial oculomotor paralysis
 - B. Duane's retraction syndrome
 - C. Internuclear ophthalmoplegia
 - D. Absence of medial rectus
- (Ans. C. Internuclear ophthalmoplegia)

Internuclear ophthalmoplegia results from lesion of MLF b/w pons (abducent nucleus) and midbrain (oculomotor nucleus). Lesion of fibres carrying the conjugate signals from abducent interneurons to the contra/L medial rectus motor neurons results in failure of adduction on attempting lateral gaze. Multiple sclerosis is the m/c cause of it.

- A child presents with unilateral proptosis which is compressible and increases on bending forwards. It is non-pulsatile and has no thrill or bruit. MRI shows retroorbital mass with echogenic shadows. The most probable diagnosis is ?

[AIIMS May'10]

- A. Orbital varix
- B. Orbital Encephalocele
- C. Orbital A-V malformation
- D. Neurofibromatosis

(Ans.: A. Orbital Varix)

Orbital varix is c/by unilateral, compressible proptosis which is non pulsatile and has no thrill or bruit. Increasing venous pressure (forward bending, defecation) precipitates the condition. Echogenic shadows in MRI are d/to formation of phleboliths.

If thrill or bruit is found AV malformations are likely.

- A young adult presents 2 days after trauma to the eye with proptosis and pain in the right eye. O/E, he is found to have a bruise on the right eye and forehead. The most likely diagnosis is [AIIMS Nov'11]

- A. Fracture of sphenoid
- B. Carotico-cavernous fistula
- C. Cavernous sinus thrombosis
- D. ICA aneurysm

(Ans.: B. Carotico-cavernous fistula)

Carotico-cavernous fistula (CCF) are common after penetrating/closed injury to eye.

- Patient comes with headache and bitemporal hemianopia with 6/6 vision. It may be due to:

[AIIMS Nov'09]

- A. Trauma
- B. Lesion at chiasma
- C. Bilateral cavernous lesion
- D. Toxic neuropathy

(Ans. B. Lesion at chiasma)

Bitemporal hemianopia is seen in lesions of optic chiasma which can be d/to craniopharyngioma, suprasellar/pituitary tumours)

- A 25 year old male comes with bilateral ptosis and restriction of eye movements. He has no squint and no diplopia. It may be due to:

[AIIMS Nov'09]

- A. Myasthenia gravis
- B. Thyroid myopathy
- C. Multiple cranial nerve palsy (Mobius syndrome)
- D. CPEO

(Ans. D. CPEO)

CPEO is pure progressive external ophthalmoplegia in <20 yrs. Patient often presents with ptosis and symmetrical weakness of extra-ocular m/s.

CPEO plus is CPEO + neurological manifestation. Kearns-Sayre syndrome is a subset of it.

- A tennis player gets hit by a ball in the face followed by decreased vision. It may be due to:

[AIIPGMEE 2011]

- A. Optic neuritis
- B. Pars planitis
- C. Vitreous detachment
- D. Equatorial edema

(Ans. A. Optic neuritis)

The player has sustained contusion over eyeball which can lead to traumatic optic neuropathy with subsequent poor vision.

- A patient with clinically significant diabetic macular edema with NPDR was treated with macular grid photocoagulation. The patient still has macuo-vitreous traction. Preferred t/t is:

[AIIMS May'11]

- A. Intravitreal bevacizumab
- B. Pars plana vitrectomy
- C. Repeat macular grid photocoagulation
- D. Augmented macular photocoagulation

(Ans. B. Pars plana vitrectomy)

Pars plana vitrectomy is TOC for complicated vitreo-macular traction. If left untreated it can lead to RD.

- A 25 yr old female presents with recurrent chalazion. Curratage should be done to rule out which of the following condition. [AIPGMEE'12]

- A. Sebaceous cell adenocarcinoma
- B. Basal cell carcinoma
- C. Squamous cell carcinoma
- D. Lymphoma

[Ans.: A. Sebaceous cell adenocarcinoma]

The malignant sebaceous gland carcinoma most commonly arises in the meibomian glands. A biopsy should be performed on all recurrent or resistant chalazia to rule out Sebaceous cell adenocarcinoma.

- A 55 yr old male on one eye shows a limbal scar, deep aqueous chamber, iridocyclitis & a dark reflex in pupillary area. His vision is 6/6 in this eye with + 11.0 D sphere glasses. The most likely diagnosis is:- [AIPGMEE'12]

- A. Hypermetropia
- B. Pseudophakia
- C. Aphakia
- D. Posterior dislocation of lens

[Ans.: B. Pseudophakia]

Limbal scar indicates past Sx on eye. When there is IOL in posterior chamber there may be deep AC, jet black pupillary reflex, and iridocyclitis.

- A patient complains of unocular diplopia. On examination with oblique illumination on slit lamp a golden crescent is seen in pupillary area and on coaxial illumination a dark crescent is present. Most likely d/g is [AIPGMEE'12]

- A. lenticulus
- B. Microspherophakia
- C. Subluxation of lens
- D. Coloboma of lens

[Ans.: C. Subluxation of lens]

In dilated eyes, on focal illumination shining golden crescent sign is seen in subluxation of lens. On distant ophthalmoscopy it appears as dark line.

NOTES

ANATOMY & PHYSIOLOGY

EXTERNAL EAR

- *Eustachian tube (Auditory tube)*
 - Outer or lateral 1/3rd is bony and medial 2/3rd is cartilaginous (opposite of EAM).
 - Blood supply : Ascending pharyngeal artery, middle meningeal a., artery to pterygoid canal.
- *External auditory meatus (EAM or EAC)*
 - Outer 1/3rd is cartilaginous and inner 2/3rd is bony. Anterior wall is shorter than posterior wall. Total length is 24 mm. In neonates, virtually there is no bony EAM.
 - Posterior wall & floor of EAM is s/by auricular br. of vagus (**Arnold's nerve**). Stimulation of this nerve during cleaning of wax causes cough reflex.
 - **Nerve of Wrisberg** supplies postero-sup part of EAC.
- **Anaesthetic ear canal** : Absence of sensation over postero-superior part (*Hitzelberg sign*).

Pinna

- Made of single cartilage developed from 1st & 2nd arch (by 6 Hillock of His)
- Failure to fuse these hillocks results in **preauricular sinus** (m/c site of which is tragus & ant. crus of helix)
- Abnormal shapes of pinna are noted in bat ear (antihelix poorly formed, large chonchae), Wildermt's ear, and Mozar ear
- Surgical reconstruction is done at preschool age by rib cartilage.
- Pinna (Ear lobule) is s/by greater auricular nerve and lesser occipital (C2-3), vagus, auriculotemporal, facial nerve.
- For anotia, microtia, and canal atresia minimal age of surgery is 7 yrs.

Mac Ewen's triangle

- Also k/as *supra-meatal triangle*. An area in the mastoid antrum of temporal bone.
- Spine of Henle is situated in the triangle. It is a surface landmark of mastoid antrum.
- Boundries-
 - Above : Supramastoid crest
 - Ant. : Ext. meatus
 - Posteriorly: Vertical tangent to posterior meatus.

Cymba concha

Clinical landmark for mastoid *antrum* (site of tenderness in acute mastoiditis)

→ *Antrum is the largest and consistent air cell*

MIDDLE EAR (TYMPANIC CAVITY)

- Develops from 1st pharyngeal pouch + dorsal end of 2nd pouch in 4th week of IUL
- 3 parts---
 - Epitympanum or attic
 - Mesotympanum
 - Hypotympanum
- **Protympanum is eustachian tube area**
- Middle ear *cleft* is middle ear + eustachian tube + aditus + antrum + mastoid air cell
- Mastoid process develops after 1st yr of life
- *Korner's septum* is bony plate separating the superficial squamous cell from deep petrosal cell in mastoid.
- *Middle ear ossicles*
 - Outer to inner there are 3 ear ossicles: MIS (Malleus, incus & stapes).help sound transmission for hearing.
 - Weight of the middle ear ossicles are as follows:
 - Malleus 25mg ; Incus 27mg; Stapes 3mg
 - Stapes is horse shoe shaped and is smallest.

Internal acoustic meatus (IAM)

- Length is 8-10 mm
- There are 4 quadrants; each poses one nerve
 - Anterosuperior (facial), anteroinferior (chochlear), posterosuperior (superior vestibular), posteroinferior (inf. vestibular)
- Vertical crest in the fundus of IAM is k/as *Bill's bar*. Bill's bar is the surgical landmark for facial nerve identification during translabyrinthine surgery.

Inner ear (Labyrinth)

- Inner ear lies in the **petrous** part of temporal bone
- There are 3 semicircular canals (SCC) anterior, posterior and lateral. 3 SCC open into utricle through 5 openings.
 - Anterior and posterior SCC have joint opening in the utricle. 3 canals lie at 90° to each other.*

Nystagmus is horizontal from horizontal SCC, rotatory from the superior SCC, and vertical from the posterior SCC

- **Cochlea** : Spiral canal which takes **2 and $\frac{3}{4}$ turns** around central axis called *modiolus*. Basal coils of it responds to higher frequencies while apex respond to lower frequencies of sound.
- **Organ of Corti**
 - Is end organ of hearing located in the cochlear duct
 - Contains *endolymph*, **hair cells**, supporting cells of **Hensen's**, Dieter's cells and Claudius cells
 - Endolymph is rich in K^+
- *Outer hair cells* produce otoacoustic emissions (**efferent**), acts as modulator & more sensitive to ototoxic drugs and noise
- *Inner hair cells* are meant mainly for hearing (**afferent**), less in numbers.
- There are two main fluids in the inner ear
 - **Endolymph** is secreted by cells of stria vascularis of cochlea and by dark cells of utricle and SCC (rich in K^+)
 - **Perilymph** is found in scala vestibuli and scala tympani and it contains high Na^+ and low K^+ (like ECF).
- **Cochlear aqueduct** connects scala tympani to CSF.
- **Endolymphatic duct** is f/b by union of 2 ducts, one each from the saccule & the utricle. Its terminal part is dilated to form endolymphatic sac.
- *Hyrtil's fissure* is an embryonic remnant also k/as tympano-meningeal hiatus as it connects mesotympanum to the CSF of sub-arachnoid space. It is a transient anatomic landmark in the developing fetal petrous temporal bone and is an unusual cause of a perilabyrinthine CSF fistula, congenital CSF otorrhoea, & meningitis.

Balance of body

Vestibular apparatus / inner ear - detects position of head in space. The SCC are the body's balance organs, detecting acceleration in the three perpendicular planes.

These accelerometers make use of hair cells similar to those on the organ of Corti, but these hair cells detect movements of the fluid in the canals caused by angular acceleration about an axis perpendicular to the plane of the canal.

Feature	Utricle	Sacculle	SCC
Sensory receptor	Macula (Otoliths)	Macula (Otoliths)	Cristae
Function as	Static balance, Percieves position of the head in space		Balance organ, detects acceleration in 3 planes
Respond to	Horizontal balance (Linear balance)	Vertical balance (Linear balance)	Angular acceleration

→ Otolith membrane of macula is made up of $Ca (CO)_3$ crystals.

→ SCC detects angular (rotatory) while otoliths detect linear acceleration.

PINNA/AURICLE

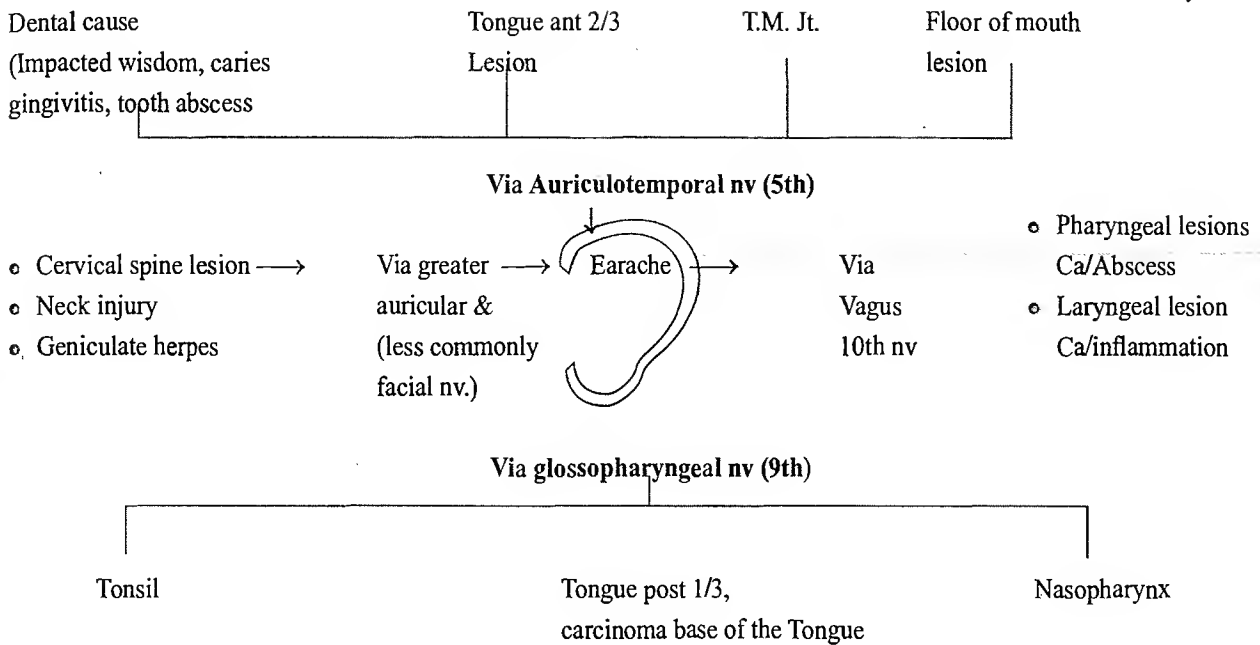
- *Hamartoma of the auricle*
May results in *cauliflower ear*
- *Perichondritis of the auricle*
Pinna is extremely tender and hot. Lobule is spared.
M/c pathogen :- *Pseudomonas*, *S. aureus*. Treated by systemic antibiotics

DISEASES OF EXTERNAL EAR

- **Wax/ cerumen** is softened by instillation of saturated solution of sodabicarb.
- **Syringing** is done by aural syringe with sterile water at body temperature. Needle is directed **postero-superiorly**.
- *Auditory tube*
Also k/as eustachian tube (pharyngotympanic tube) connects the middle ear cavity with the nasopharynx.
- *Turkey ear*:
Ear lobe with redish indurated plaque. A sign of *lupus vulgaris*.
- *Erysipelas of Pinna*
D/to streptococci or staph aureus.

→ In *keratosis obturans* --- external canal is filled up by cholestatoma mass

Referred Causes of Earache



Furunculosis of external ear

- o Staphylococcal infection of hair follicle in outer 1/3 of EAM (cartilaginous part)
- o Common in diabetic.
- o Usually single.
- o **Clinically**: painful to insert speculum & posterior auricular groove is obliterated.
- o T/t: Wick soaked in 10% ichthammol in glycerine and Neomycin - steroid ointment.

- Griesinger's sign is seen in lateral sinus thrombosis (d/to thrombosis of mastoid emissary vein & produce edema over mastoid)
- Sigmoid sinus lies close to mastoid part of temporal bone (i.e. opens extracranially) & thrombosis of S~ always secondary to infection of middle ear.
- In caloric test lateral (horizontal) semicircular canals are stimulated.

Acute otitis Externa (AOE) or swimmer's ear or Singapore ear

- o D/to *pseudomonas pyocyanea*, *staph*, *strepto*.
- o Ear is painful (tragus is extremely tender ---positive tragus sign) & pruritus is present.

Malignant Otitis Externa

- o NOT a malignancy
- o Caused by ***Pseudomonas***. (or *Aspergillus*)
- o Seen in **diabetic**, immuno-compromised & elderly.
- o C/f: Severe pain, blood stained ear discharge.
- o C/c: Meningitis, sinusitis, temporal lobe cerebritis; facial nerve palsy (other CN involved 9, 10, 11)
- o T/t: Aural toilet, systemic antibiotics (Ceftazidime / fluoroquinolone ± aminoglycoside)
- o *Otitis externa hemorrhagica* / *Bullous myringitis*
Hemorrhagic blebs on TM a/w influenza epidemic.

TYMPANIC MEMBRANE (TM)

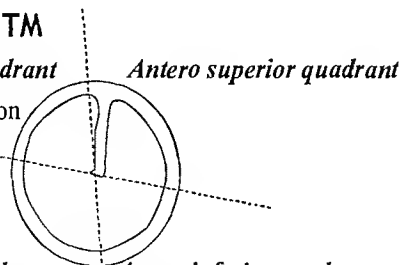
- o Tympanic membrane (TM) separates the external ear from the middle ear
- o TM is horizontal in infants
- o Total surface area is 85 sq mm & out of which only 55mm² (vibrating area is 55 sq mm) is functional area stapes footplate is 3.2 mm². area ratio or HYDRULIC RATIO IS 17:1
- o The TM is situated at an angle of 55° with both floor and anterior wall of the EAM.

- Longest diameter is 9-10 mm (postero-superior to antero-inferior).

Quadrants of Rt. TM

Postero-superior quadrant

- Marginal perforation
- Atelactic drum



Postero-inferior quadrant

- For curvilinear incision in Acute OM
- Myringotomy for ASOM
- For radial incision

Antero-inferior quadrant

- Cone of light is seen
- Myringotomy for glue ear / serous OM (Site of Grommet insertion)
- M/c site of perforation in ASOM

- Central perforation of TM (involving -- safe CSOM pars tensa) signifies
- Marginal perforation of TM is seen in -- unsafe CSOM
- Attic perforation (occurs in pars -- unsafe CSOM flaccida of TM) signifies
- Total perforation of TM signifies -- unsafe CSOM
- Hemorrhagic blebs on TM -- Bullous myringitis (during are seen in influenza epidemic)
- Vesicles on TM are seen in -- Herpes-zoster oticus
- Retraction pockets & -- Barotraumatic otitis media air-bubbles are seen in
- Cartwheel pattern of TM is -- ASOM seen in

- There is large surface ratio between tympanic membrane and oval window (about 35) and the ossicle system lever gain (about 1.32).

Traumatic perforation of TM

- Perforation with irregular margins of TM
- T/t : No t/t required

- M/c cause of acute tonsillitis → *Streptococcus hemolyticus*.
- M/c cause of epiglottitis → *H. influenzae* (but GABHS in children as per latest data).
- M/c cause of acute necrotising OM → *Streptococcus hemolyticus*.

DISEASES OF MIDDLE EAR

Acute Otitis Media (AOM/ ASOM)

- Common in 3 month - 3 year children
 - Degree of pneumatisation of the mastoid bone is an important factor in severity of clinical manifestations
 - Usually follows URI. M/c organism :- *S. pneumoniae* (35%) and *H. influenzae*
 - On otoscopy -- "cartwheel pattern" of TM
 - Pulsatile otorrhea and 'light-house sign' are seen in stage of suppuration. Sand reservoir sign +ve.
 - M/c intracranial c/c -- meningitis
 - T/t - 90% spontaneous healing. Penicillin V (oral) or Ampicillin (in children) are DOC.
- If TM is bulging or if pain persisting and other symptoms are severe or persistent --- Myringotomy.

Secretory OM / Serous OM / Glue Ear / OME

- Non-suppurative OM which is also k/as *catarrhal / secretory OM / otitis media with effusion*
- Common in school going children
- Presuppurative stage of AOM may progress to OME
- Cultures of middle ear often - ve (non - purulent effusion in the middle ear cleft)
- M/c presentation is conductive deafness with 25 dB hearing loss, (m/c cause of conductive deafness in children)
- TM : Intact, lusterless / retracted, sometimes pinkish. Fluid level / air bubbles are seen rarely but are characteristic
- T/t - In most persistent cases -- Myringotomy + suction
 - If recurrent effusion is there --- Myringotomy + ventilation tube (grommet) insertion
 - Chymotrypsin instillation helps in drainage.

Adhesive OM (Healed / Inactive OM)

- Permanent structural changes in middle ear cleft following healing / inactivation of OM.
- CI/f - Dry perforation
 - Atelectic drum (esp. in posterosuperior segment)
 - Tympanosclerosis : Chalky deposit and hyaline changes, fixation of ossicular chain.

Acute Necrotizing OM

- Rare d/s seen after some exanthems e.g. measles, scarlet fever, influenza, typhoid fever, etc. Infecting organism is β-hemolytic streptococci
- There is profuse, purulent, otorrhea. It may lead to secondary cholesteatoma

Tuberculous OM

- C/by painless ear discharge, multiple perforations, and facial nerve palsy

CSOM

- Safe CSOM: Tubotympanic (Central perforation) - Profuse and mucoid discharge
- Unsafe CSOM: Tympanomastoid and atticointral variety - Purulent bloody discharge
- M/c bacteria --- Pseudomonas > mixed
- T/t of safe variety

1. Active stage—suction clearance under operating microscope.
2. If discharge is persistent after t/t and mastoid reservoir phenomena (hazy air cells) is present on X-ray →

Cortical mastoidectomy (Schwartz's operation)

3. Quiescent stage --- Only to control cold and allergy.
4. Inactive stage --- Myringoplasty.

- Pearly white mass behind intact TM in a young patient with conductive HL is seen in --- Congenital cholesteatoma.
- Postero-superior retraction pockets are formed in --- 1^o cholesteatoma.
- Marginal perforation is seen in --- 2^o acquired cholesteatoma.

T/t of unsafe variety

1. If cholesteatoma does not involve mesotympanum .Unsafe CSOM is a/w atticoantral d/s or hearing loss or facial nerve palsy or vertigo or labyrinthine fistula (+ve fistula sign) → *MRM*

2. Unsafe CSOM + Brain abscess → *Refer to neuro surgeon*

Unsafe CSOM + Subdural empyema → *Burr hole Sx*

Unsafe CSOM + Hydrocephalus → *VP shunt*

3. When sensory-neural deafness present (inner ear involved) → *Radical Mastoidectomy*

4. If ossicular chain is disrupted in cholesteatoma, mastoiditis without c/c → *Tympanoplasty*

C/c

- Brain abscesses (esp. in temporal lobe).
- Mastoid abscess (M/c extracranial complication).
- Lateral sinus thrombophlebitis (char/by Picket fence fever with rigors, recurrent otorrhoea, delta sign on x-ray & Griesinger's sign d/to edema over mastoid).
- Infection from CNS/meninges spreads to labyrinth via **cochlear aqueduct**.

→ M/c site of congenital cholesteatoma --- Petrous part of temporal bone (TM is normal)

→ M/c site of acquired cholesteatoma --- Prussack's space / attic area

→ M/c intracranial c/c of CSOM --- Brain abscess (temporal lobe abscess).

→ M/c effect/ complication of CSOM --- Hearing loss.

→ M/c nerve involved in CSOM --- Facial nerve.

Subperiosteal abscesses in relation to mastoid infections

1. *Post auricular abscess* --- M/c type. Occurs over mastoid bone (in children over MacEwan's Δ)
2. *Meatal / Luc's abscess* --- Pus breaks through the bony wall b/w antrum and EAM from zygomatic cells
3. *Citelli's abscess* --- In digastric D (behind mastoid along posterior belly of digastric)
4. *Bezold's abscess* --- In sternocleidomastoid sheath
5. *Zygomatic abscess* --- Along zygomatic bone (ant.)
[mnemonic L/M, C/D, B/S Love / My College / During Biochem / Session]

ASSESSMENT OF HEARING

Tympanic Function Tests (TFTs)

	Conductive HL	SNHL
• Rinne's	-ve (BC > AC)	+ (AC > BC)
• Weber's	Lateralization to poor / diseased ear	To better ear
• ABC	= to examiner	↓ compared to examiner
• Schwabach's	↑	↓
• Gelle's	-ve	+ve
• Binge	-ve	+ve

Rinne's Test

- If AC > BC (Positive) – Normal, SNHL, Presbycusis
- If BC > AC (Negative) – Conductive deafness (CSOM)
- False +ve Rinne's is seen in --- SNHL
- False -ve in --- Dead ear, severe unilateral SNHL d/to transcranial transmission of sound to other ear.

In conductive deafness no change (Bing -ve) while in normal person or with SNHL hears louder when ear canal is occluded and softer when open (Bing +ve)

- On PTA if $AC > BC$ in right ear, $BC > AC$ in left ear, Weber lateralized to right --- Dead ear or severe SNHL
- On PTA if $AC > BC$ in both ear, Weber lateralized to left --- B/L SHL but more in left
- On PTA if $BC > AC$ in both ear, Weber lateralized to left, ABC normal in both --- B/L CHL but more in left

Audiometry

Pure tone audiometry (PTA) :

PTA is the commonest audiometry

- Human speech ranges from 300 to 4,000 Hz.
- A-B gap with Carhart's notch at 2000 Hz in B.C. suggests --- otosclerosis.
- Frequency which can cause temporary hearing loss (noise induced hearing loss) --- 2000-4000 Hz.
- Sudden dip at 4000 Hz in both AC and BC suggests --- acoustic trauma. (noise induced hearing loss)
- Roll over phenomena/curve is typical of --- retrocochlear lesion. On ↑ing the intensity of sound discrimination falls further.
- Rising type curve is typical of --- Meniere's d/s

Cochlear Vs Retrocochlear lesions

	Cochlear	Retrocochlear
• Site of lesion	Cochlea	Distal to cochlea
• Tone decay	-	+ (10 sec)
• Recruitment	+	-
• Curve type	-	Roll over curve

Impedance audiometry & Tympanograms

Used to assess middle ear functions in children. It includes tympanometry and acoustic reflex assesment.

Types of tympanogram

- Type A -- Normal
- Type As -- In otosclerosis or malleus fixation
- Type Ad -- In thin or lax TM
- Type B -- A flat /dome shaped graph, seen in thick TM or middle ear effusion (OME)
- Type C -- In retracted TM
- Type D -- High flat curve seen in perforation of TM
- Negative curve -- Glue ear (OME)

Evoked response audiometry (ERA)

ERA is a newer advancement, objective test. U-shaped audiogram indicates congenital deafness.

Special Test of hearing

• Recruitment

- Is a phenomenon of abnormal growth of loudness.
- Ear which does not hear low intensity sound begins to hear greater intensity sound as loud.
- Seen in lesion of cochlea (i.e. Ménière's disease, presbycusis). These are poor candidate for hearing aid.

• BERA (Brainstem evoked response audiometry)

IOC for assessment of hearing loss in neonates/ infants of congenital deafness, mental retardation, CPA tumours (acoustic neuroma) etc. The waves detected in BERA tests are :-

1. Auditory nerve
2. Cochlear nucleus
3. Superior olivary complex
4. Lateral lemniscus
5. Inferior colliculus (denoted by V wave)
- 6 and 7. Medial geniculate body

• CERA (Cortical evoked response audiometry):

BERA covers whole auditory pathway but does not cover cortex for which CERA c/b used.

- Initial screening test for hearing assesment in newborns is done by OAE (Oto-Acoustic Emission produced by outer hair cells of cochlea) test.

→ Loudness of sound is measured by its intensity.

→ Travelling wave theory is most accepted theory of sound transmission

Tests of vestibular function

Caloric test (Fitzgerald and Hallpike technique)

- Based on thermal stimulation of lateral (horizontal) SCC with water. Results recorded on a calorigram
- Cold water induces nystagmus to opposite side and warm water same side (mnemonic COWS-cold opposite, warm same)
- In canal paresis duration of nystagmus is reduced for both hot and cold (signifies peripheral vestibular lesion)
- If labyrinth is dead no nystagmus will be elicited from any ear
- Cold air caloric test (Dundas Grant test) is used when there is perforation of TM

- Ext. ear is irrigated with 30°C and 44°C water.

Kobrak's test

i.e. cold caloric test with ice cold water

Fistula test :

- Positive test is indicated by vertigo and nystagmus.
Positive fistula test is seen in--- Erosion of horizontal SCC by any *fistula* (i.e. cholesteatoma, fenestration operation). False +ve test in absence of fistula, is seen in congenital syphilis
- Negative ---indicates absence of fistula on lateral SCC (Normal, dead labyrinth d/to old labyrinthitis)

Tests used to differentiate cochlear deafness from neural deafness

- These are the tests used to differentiate vestibular end-organ function and vestibular nerve function.
- BERA , Recruitment test, & SISI are +ve in cochlear d/s
- Tone decay test, speech discrimination score (90 to 100%) are +ve in retrocochlear (neural) d/s .

Hearing Dysfunction

Tullio phenomena

Vertigo is produced by loud sounds. It is seen in congenital syphilis, or when 3 functioning windows are present in ear e.g. in fistula of SCC, fenestration operation in the presence of mobile footplate of stapes.

- Pulsatile swelling on peritonsillar region suggests --- *Aneurysm of external carotid artery*
- Pulsatile tinnitus is seen in --- *Glomus tumour, palatal myoclonus*
- Pulsatile otorrhea is seen in --- *ASOM*
- Fluctuating hearing loss is seen in --- *Meniere's disease*
- Earache worsening at night is seen in - *Malignancy*

Monaural diplacusis

Person hears 2 voices d/to pathology in one ear. Seen in lesions of cochlea, Ménière's disease

Presbycusis

Person hears better in noisy surrounding .Seen in old age d/to degeneration of hair cells in cochlea.

Paracusis Willis

Better hearing in noisy surrounding seen in *otosclerosis*

- Hyperacusis---Normal sound is heard noisy (seen in *stapedial muscle paralysis*)

Tinnitus

- M/c cause of Tinnitus ----- Impacted cerumen
- M/c type of Tinnitus ----- Subjective.
- Objective tinnitus is seen in --- glomus tumour, palatal myoclonus, patulous ET, TMJ abnormality, spontaneous OAE, AV malformations

- M/c C/c of otitis media --- Conductive hearing loss
- M/c cause of conductive hearing loss --- Impacted cerumen
- M/c cause of conductive hearing loss in elderly --- Otosclerosis
- M/c cause of sensorineural hearing loss --- Presbycusis
- M/c cause of vertigo --- Physiological
- M/c pathological cause of vertigo --- BPPV i.e. benign paroxysmal positional vertigo BPPV

DISEASE OF INNER EAR

LABYRINTH DYSFUNCTION

- Include -
 - Meniere's d/s
 - Vestibular neuritis
 - BPPV

MÉNIÈRE'S DISEASE

- Also k/ as **endolymphatic hydrops**.
- More common in males. A/w syphilis.
- A Meniere's disease gene linked to chromosome 12p12.3.
- Disorder of inner ear where the endolymphatic sac is dilated , endolymph secretion is ↑ and scala media (cochlear duct) and saccule are mainly affected.
- Patho: ↑endolymph production and ↓ in absorption.
- C/I/f
 - Commonly affects 35-60 year males. D/s is usually unilateral
 - Triad of
 - Episodic **vertigo** + u/L fluctuating/ episodic **deafness** (hearing loss) + **Tinnitus**
 - There is also sense of fullness or pressure in the ear
- C/I/tests
 - **Tullio phenomena** (loud / noise produce vertigo d/ to

distended saccule lying against the stapes footplate)

- Recruitment (intolerance to loud / amplified sounds)
- Diplacusis (distortion of sound)

o *Inv:*

- PTA show sensorineural hearing loss with loss of lower frequencies (**rising type curve**)
- SISI score >70% (normal <15%)
- Tone decay test >20 dB
- Electrocochleography- SP/AP ratio >30%

o *T/t*

- T/t of vertigo (Vasodilators/ nicotinic acid, betahistine)
- Cawthorne's head exercises
- Meniet device (intermittent inner ear pulse pressure)
- Surgery (stellate ganglion block, Singular/ vestibular neurectomy ; Donaldson's repair).
- Microwik
- Dexamethasone for pt with sudden SNHL

Lermoyez syndrome

A variant of Meniere's d/s with reversal of symptoms. SNHL improves suddenly during attacks of vertigo.

Cochlear hydrops

Only cochlear symptoms are present. There is no vertigo.

BPPV

- o Benign paroxysmal positional vertigo (BPPV) is the m/c disorder of the inner ear's vestibular system.
- o BPPV produces a sensation of spinning called vertigo that is both paroxysmal and positional, meaning it occurs suddenly and with a change in head position.
- o Cause : result of otoconia, tiny crystals of calcium carbonate that are a normal part of the inner ear's anatomy.
- o Appley's test is done

ACOUSTIC NEUROMA

- o Also called *vestibular schwannoma*.
- o Benign tumour which arises from neurilemmal sheath of the **superior vestibular nerve/VIII nerve** (Acc/to Logan Turner book of ENT and Schwartz)
- o Affects 40-60 yrs of age. Comprises 80% of all cerebellopontine angle tumour (**m/c CPA tumour**)
- o B/L acoustic neuromas are pathognomonic for NF-2
- o *Cl/f*
 - U/L progressive deafness (SNHL) with tinnitus is first/earliest presenting symptom.

- Balance difficulty
- CN-5 (**trigeminal**) is involved earliest with ↓corneal sensitivity. (↓ **or -nt corneal reflex** is the earliest sign)

o *TFT*

- *Hitzelberger's sign* → Hypoesthesia of posterior meatal wall.
- *Roll over phenomenon* is seen
- Threshold tone decay test show *retro cochlear type* of lesion.

- o *D/g* – **MRI** is gold standard for d/g.. BERA is preferred audiological Ix.

- o *T/t* – Surgery is TOC. Gamma knife (stereotactic radiotherapy) is the recent advancement. Rehabilitation of SNHL in case of b/L acoustic schwannoma is done by brain stem implant in lateral recess of 4th ventricle.

- o *C/c* - Surgery risk include facial palsy, dead ear

Glomus jugulare

- o K/as chemodectoma (non- chromaffin para-ganglioma).
- o Fisch classification is based on extent.
- o Tumour of jugular vein (**m/c benign tumour of middle ear**)
- o The tumor was located primarily in the area of the **promontory**, but can extend to the hypotympanum.
- o **M/c** symptom is hearing loss, but **pulsatile tinnitus** is most significant symptom. Brown's sign is positive, which is tumour blanches on air pressure/spiegelisation)
- o 'Rising sun sign' (Reddish mass behind TM) on otoscopy.
- o "**Phelp's sign** " (Erosion/loss of bony septum b/w carotid canal & jugular foramen) is a radiological sign seen in CT.

→ *Glomus tumour is tumour of paraganglionic cells.*

→ *M/c site of glomus tumour—Fingers.*

→ *Glomus jugulare & glomus tympanicum* —are vascular neoplasm that usually arises from jugular bulb & tympanic plexus, respectively. Both tumours spread cephalically & posteriorly into the middle ear & mastoid.

Both are non-chromaffin producing paragangliomas & histological same as carotid body tumour.

→ *Glomus vagale*— neoplasm arising in skull base & neck may extend superiorly into the cranial vault.

→ *Pulsatile tinnitus* is classically seen in glomus tumour of ear.

→ "*Lyre sign*" is splaying of ICA on ECA d/to carotid body tumour.

OTOSCLEROSIS

- Also k/as Otospongiosis which is active stage of otosclerosis.
- AD inheritance.
- Ankylosis of the foot plate of the stapes (fixation of stapes) d/ to new vascular spongy bone formation.
- M/c site of involvement - anterior edge of oval window (area of fistula ante fenestrum)
- CI/f : Female presenting with gradually progressive, conductive hearing loss usually B/L. Paracusis willisii, tinnitus, absent stapedial reflex.
- On otoscopy --- TM is normal and mobile. **Schwartz sign** (reddish hue or flemmingo pink reflex seen through the intact TM d/to vascular otospongiotic mass). Blue Mantle of Manganese is also seen. Schwartz sign is seen in early stages of d/s & its presence is a contraindication to stapes surgery.
- TFT shows -ve Rinne test.
- On pure tone audiometry loss of air conduction more for lower frequencies. Carhart's notch is dip in bone conduction curve maximum at 2000Hz.
- T/t :
 - Surgical - **Stapedectomy** with hearing aid (prosthesis replacement) is TOC.
 - Medical - Sodium fluoride used sometimes when Schwartz sign is +ve. It arrests further cochlear loss by ↓ ing the osteoclastic activity, inhibiting proteolytic enzyme in cochlea, and ↑ ing osteoblastic activity.
- D/s is more active during pregnancy.

Hearing Aids (HA)

- HA contain :
Microphone + Amplifier + Receiver.
- HA are mainly used to amplify the sound.
- Bone anchored hearing aids (BAHA) are used for:-
 - Absent pinna (Anotia)
 - Canal stenosis
 - EAC atresia
 - Discharging ear

Cochlear implants (CI)

- CI contain :
Microphone + Amplifier + Electrodes.
- All implants have microphones, external speech processors, signal-transfer hardware, transmitters, receivers, and electrodes. Each plays an important part in converting mechanical sound to an electrical stimulus.
- CI are the first true bionic sense organs

- CI are not the hearing aids, which only amplify the sound
- CI are 2 types:
 - Single channel
 - Multi channel (better)
- Pediatric implantation is indicated in children ≥ 12 months with bilateral severe-to-profound SNHL with pure tone averages of ≥ 90 dB in the better ear.
- The transmitter, or outer coil, is placed on the mastoid (usually held in place by magnets) and sends the processed signal to the receiver via radiofrequency. The receiver, surgically placed in a well over the mastoid, receives the signal and sends electrical energy to one or many electrodes in the array. The electrode array, which lies within the cochlea (in scala tympani), delivers the electric signal to electrodes along its length. Electrode array are inserted in cochlea by cochleostomy.
- Contraindications:**
An absent cochlear nerve is an absolute contraindication. The absence of the cochlea (Michel deformity), and a small internal auditory canal (a/w cochlear nerve atresia), active middle ear d/s, are contraindications to implantation on that side. Labyrinthitis is a relative contraindication. Neurofibromatosis II, mental retardation, psychosis, organic brain dysfunction, and unrealistic expectations may also be contraindications.
Other forms of dysplasia are not necessarily contraindications. However in patients with cochlear dysplasia CI are a/w ↑ risk of poor result, CSF leak, and meningitis.
- Studies have shown that CI are a/w better speech perception, speech production, and language development in prelingually deaf children.

NOSE

OPENINGS IN LATERAL WALL OF NOSE

Opening of	Opens in / Meatus of nose
Sphenoidal sinus →	Spheno-ethmoidal recess
Posterior ethmoidal sinus →	Superior meatus
Anterior ethmoidal sinus →	Ethmoidal infundibulum (Hiatus semilunaris) of
Frontal sinus →	Middle meatus
Maxillary sinus →	Middle meatus
Middle ethmoidal sinus →	Middle meatus
Fronto-nasal duct (FND) →	Middle meatus
Nasolacrimal duct (NLD) →	Inferior meatus

- Chronic dacryocystitis & mucocele of lacrimal sac are treated by dacryocystorhinostomy. In dacryocystorhinostomy lacrimal sac is drained in ---- middle meatus (via frontonasal duct)
- In Prof puncture / antral puncture maxillary antrum is punctured & drained through ---- inf. meatus
- In intra nasal antrostomy (for chronic suppurative maxillary sinusitis) opening is made in ---- inf. meatus
- Osteomeatal complex is an important landmark during FESS. It includes middle meatus + uncinat process + ethmoidal bulla
- Concha bullosa ---- pneumatized middle turbinate
- Drainage of nasal mucosa is caused by --- ciliary movements

Nasal septum is formed by

Bony part

V	E	S	P	NF
↓	↓	↓	↓	↓
Vomer	Ethmoid's Perpendicular plate	Sphenoid Rostrum	Palatine	nasal spine of Frontal bone

Cartilaginous part

M	A	S
↓	↓	↓
Maxillary	Alar cartilage	Septal Cartilage

- **Nasal valve** is narrowest part of nose, produces most turbulent flow. *Formed by* --- Lower edge of upper lateral cartilage, anterior end of inferior turbinate, adjacent NS with surrounding tissues.
- **M/c site of epistaxis** --- **Little's area**. (Situated in antero-interior quadrant of nasal septum) Sphenopalatine artery is k/as artery of epistaxis
[Note. that posterior ethmoidal artery does **not** take part in formation of *Klesseilbach's plexus* around Little's area]
- **Woodroff plexus** --- Venous plexus situated at posterior end of inferior turbinate on the lateral wall of nose. There is anastomosis b/w sphenopalatine & pharyngeal vein.

Nasal mucosal membrane in

- Chronic hypertrophic rhinitis --- Mulberry appearance
- Atrophic rhinitis (Ozaena) --- Mucosa is lined by stratified squamous epithelium. Roomy nose filled with crusts
- Rhinosporidiosis --- Pink/ purple polypoidal mass protruding through nose (mulberry appearance)
- Mucormycosis --- **Black necrotic mass** filling nose
- Coryza --- Congested

- Maxillary sinusitis --- Red and swollen
- Allergic rhinitis --- Pale and swollen

Rhinolalia

- Rhinolalia Clausa
 - A/w hyponasality.
 - Seen in angiofibroma
- Rhinolalia Aperta
 - A/w hypernasality.
 - Seen in --- Cleft palate, palatal palsy

Granulomatous/ chronic diseases of nose

	Nose	Nasal septum
○ Syphilis	Snuffles, Saddle nose	Perfora ⁿ (bony part)
○ Leprosy	Nasal bleed, Saddle nose	Perfora ⁿ (cartilage destruction)
○ Lupus vulgaris	Begins in vestibule, Apple jelly nodules	Perfora ⁿ (cartilagenous part)
○ SLE	Ala of nose involved	Perfora ⁿ (cartilagenous part)
○ Sarcoidosis	Nasal bridge collapse	Perfora ⁿ of anterior portion of NS
○ WG	Nasal block/crust/ bleed	Total destruction of NS
○ TB		Septal perforation

- *Wegner's granuloma* is a midline destructive lesion of nose which causes total destruction of nasal septum.
- Trauma is the m/c cause of perforation of nasal septum.
- All granulomatous diseases involve cartilaginous part.
- Nasal septal perforation has been reported as a side effect of anti-angiogenesis drugs like bevacizumab

Ozaena/Atrophic Rhinitis

- M/c organism is *Klebsiella ozaenae* / *Perez Abel bacilli*.
- Mucosa is atrophied and foul smelling crusts present (merciful / blessing anosmia)
- D/s is usually b/L; familial; seen in females of pubertal age.
- A/w --- Vitamin A deficiency, TB, syphilis, reflex sympathetic dystrophy, sex hormones, bld group O & B

- Middle turbinate is involved earliest.
- Rx :
 - Medical --- Alkaline nasal douches, Local spray of estrogen & placental extract, Kemistine solution
 - Surgical--- Young's operation, LautenSlager surgery

Rhinoscleroma (woody nose)

- Chronic granulomatous d/s of URT caused by Gram - ve coccobacillus, Klebsiella Rhinosclerema (**Frisch Bacillus**)
- Common in north India, in HIV⁺ patients
- **Mikulicz cells**⁺ (foamy histiocytes), **Russell bodies**, plasma cells present.
- Cicatrization & stenosis of anterior nares
- T/t : Cautrization, Streptomycin, TMP-SMX

Glanders :

Caused by *Pseudomonas mallei*, T/t :- Sulfadiazine

PARANASAL SINUSES

Acute Bacterial Sinusitis

- *Streptococcus pneumoniae* (33%) is the commonest organism. *H. influenzae* (25%), *Moraxella catarrhalis* (20%) are also common.
- Ix --- CT Scan
- T/t --- Amoxicillin / TMP-SMX for detected cases.

Chronic Bacterial Sinusitis

- Symptoms of sinus inflammation ≥ 3 months
- Thick & greenish discharge
- Commonest c/c :- orbital cellulitis.

Superior orbital fissure syndrome

Deep orbital pain+ frontal headache + progressive paralysis of CN 6, 4, & 3

Orbital apex syndrome

Superior orbital syndrome + optic nerve involvement + 2nd division of CN 5 involvement

Mucocoele

Presents as swelling at inner canthus below eyebrow, frontal sinus is m/c involved f/b ethmoid sinus. Mucocoele of PNS are treated by Lynch-Howarth operation.

PNS	Deve loped at	Radio logically visible at	M/c involved in	Best X-ray view
Maxillary	Birth	4-5 mo	Bacterial/ fungal sinusitis, Carcinoma	Water's
Frontal	2 yrs	6 yr	Ivory osteoma, mucocoele, osteomyelitis of frontal (Pott's puffy tumour)	Caldwell's (OF)
Ethmoidal	1 yr	1 yr, but fully devp by 8-10 yr	Acute sinusitis in children, adenocarcinoma in wood worker, SqCC in workers of nickel industry, Orbital cellulitis	Oblique
Sphenoidal	5 yrs	3 yrs	Cavernous sinus thrombophlebitis	B a s a l / lateral (SMV)

- Maxillary sinus is also k/as antrum of Highmore.
- Both the maxillary and ethmoidal sinuses are present at birth but only the ethmoidal sinuses are pneumatized.
- Order of development of sinuses (MESF) = Maxillary → Ethmoid → Sphenoid → Frontal.
- Radiologically, maxillary sinus c/b identified at 4-5 months, ethmoids at 1 year, sphenoid at 4 years, and frontals at the age of 6
- M/c sinusitis in children is --- Ethmoidal sinusitis.
- M/c sinusitis in adults is --- Maxillary sinusitis.
- For posterior ethmoidal sinus --- X-ray lateral oblique view from opp. side required
- All the sinuses are seen in lateral view.
- M/c sinus to develop :
 - Mucocoele → Frontal
 - Carcinoma → Maxillary
 - Osteoma → Frontal
- Orbital cellulitis involve → Ethmoid sinus.

CSF Rhinorrhea

- Caused by injury (m/c head trauma) to the cribriform plate/fovea ethmoidalis.
(# ethmoid > # sphcnoid > # petrous temporal bone)
- **Spontaneous CSF leak Syndrome (SCSFLS)**
Also k/as **intracranial hypotension syndrome** or non-traumatic CSF rhinorrhea.

1. A spontaneous CSF leak is idiopathic.
 2. Classified into 2 main types, cranial leaks & spinal leaks.
 3. Causes: Up to 2/3rd are a/w CTDs like Marfan syndrome, Ehlers-Danlos syndrome and ADPKD are the three m/c CTDs a/w SCSFLS. Other causes are Arnold-Chiari malformations, absent nerve roots, causes of raised ICT (as in pseudotumour cerebri)
 4. Orthostatic headache is major symptom
 5. Empty sella syndrome is robust radiological marker in pt with SCSFL.
 6. IV Cosyntropin, a corticosteroid is used in t/t.
- IOC : Intrathecal injection of fluorescein dye and nasal sinuscopy c/b used for localization of CSF leak.
 - Olfactory slit --- Cribriform plate
 - Middle meatus --- Frontal/ethmoidal sinus
 - Inferior meatus --- Temporal bone
 - Estimation of β_2 transferrin levels in nasal discharge in CSF is confirmatory.
 - In traumatic CSF leak, when CSF and blood are mixed, double ring sign or target sign is seen.
 - T/t :
 1. Post-traumatic cases C~cases are managed conservatively by placing the patients in semi- sitting position, avoiding blowing of nose/straining and sneezing. Prophylactic antibiotics are given.
 2. Persistent cases are treated surgically.

Imp. facts about nose

- Sluder's neuralgia --- Referred pain to area below eyes. Seen in high DNS pressing middle turbinates. (Anterior ethmoidal nerve syndrome)
- Potato nose (Rhinophyma)--- D/to hypertrophy of sebaceous glands. Glandular form of acne rosacea.
- Inverted papilloma of nose (Ringertz tumour) --- Benign tumour of nose with malignant potential. Present in young adults in lateral wall of nose.
- Frog face deformity of nose /face --- Seen in nasopharyngeal angiofibroma.
- M/c cause of oroantral fistula --- dental extraction (1st & 2nd molar)
- Septoplasty is preferred surgery for DNS in all age group
- A child with u/L foul smelling discharge from nose is likely to have --- FB nose.
- During maxillary (antral) washout sudden death occurs d/ to air embolism.

Nasal alkaline douche

- Contains NaHCO_3 (30 gm), Na-Bi borate (30 gm) and NaCl (60 gm) [triple sodium] dissolved in $\frac{1}{2}$ pint of water
- Used in atrophic rhinitis (ozena) and crusting rhinitis (rhinitis sicca) to dislodge crusts
 - Proetz displacement therapy
 - Contains alcohol + glycerine + saline
 - Used in chronic atrophic rhinitis
 - Mandl's paint contain iodine + KI + glycerine + peppermint oil. Used for chronic pharyngitis
 - In nasal anaesthesia lignocaine 4% is used as spray and surface anaesthesia

Surgeries for various sinuses

- Maxillary sinus → Caldwell Luc operation. Indicated in Chronic infection of the maxillary antrum which fails to respond to non-operative treatment., exploration and to obtain a biopsy, and reduce the bulk of the tumour, in suspected carcinoma of the maxillary antrum.
- Mucocoele of frontal /ethmoid sinus → Lynch-Howarth operation.
- Maxillary antral washout: Death c/b due to air embolism.

Fungal sinusitis : Non-invasive

- Chronic sinusitis seen in immunocompetent
- M/c caused by *aspergillus fumigatus*
- Maxillary sinus is affected m/c.
- H/o asthma, polyps, allergy
- Charcot - Layden crystals⁺
- T/t : Remove fungal ball by FESS + antifungals

Fungal sinusitis: Invasive

- Acute & In immuno-compromised host, DM
- *Rhizopus*, *Mucor*, *Absidia*
- Black eschars over nose necrotic tissue
- Potentially fatal. Fungus can invade brain & orbit. Frontal lobe abscess may occur.
- T/t - Amphotericin B

- D/g of allergic (non-invasive) fungal sinusitis is made by --- Area of high attenuation on CT. allergic eosinophil mucin, type 1 hypersensitivity. It is treated by --- endoscopic removal + corticosteroids
- In diabetics m/c fungal sinusitis is zygo/mucormycosis.

Nasal Myiasis (Maggots)

- Maggots are larval stage of houseflies (*Chrysomya*).
- T/t: **Instillation of chloroform water with turpentine oil kills them.**

NASAL POLYPS

Feature	Antrochoanal	Ethmoidal
• Incidence	Less common	M/c
• Etiology	Infection	Allergy, aspirin hypersensitivity
• Arise from	Maxillary sinus/antrum	Ethmoidal air cells
• Age group	Children	Old age
• Numbers	Single, u/L project backward in post. choana	Multiple, always b/L project forward
• Recurrence	–	+
• T/t	FESS or simple polypectomy (avulsion) ↓ If recurrence ↓ Caldwell Luc operation	Topical nasal spray (Fluticasone/mometasone) T/t is usually conservative [histamine, steroids] Surgery is indicated if If 1 or 2 pedunculated polyps present → Polypectomy If multiple & sessile → Intranasal ethmoidectomy [Through middle meatus] If recurrence occur ↓ Extra nasal/external ethmoidectomy

- An antrochoanal polyp is easily removed by avulsion.
- FESS has superseded other modes of polyp removal now a days.
- Caldwell luc operation is done for recurrent polyp (avoided now-a-days).
- Nasal polyps are more common in males (2:1), incidence increases with age, they are rare <2 year of age, if present think for other d/g like meningioma.
- Samter's triad is association of asthma + nasal/ethmoidal polyposis + aspirin hypersensitivity d/o leukotrienes excess.

Rhinosporeidiosis

- It is a fungal granuloma caused by *Rhinosporidium seeberi*.
- Seen in Tamilnadu (South India) / coastal India

- M/c affects nose and presents as irregular looking nasal polyp/mass with epistaxis, pink to purple in colour (mulberry appearance).
- Mass is very vascular and bleeds on touch
It may involve skin (subcutaneous nodules), lip, palate, larynx, liver, spleen.
- Main symptom is blood stained nasal discharge
- D/g --- By biopsy (*never cultured*)
- T/t – Complete excision is TOC
– Dapsone (for recurrence)

Juvenile Nasopharyngeal Angiofibroma

- Benign tumour of nasopharynx but locally invasive
- Arises from **posterior part of nasal cavity near sphenopalatine foramen**
- It occurs mainly in young males in second decade (12-20 years is m/c age group)
- Role of sex hormones (testosterone) in etiology.
- **Patho:** high vascular tumour (with no m/s coat in vascular channels, so heavy bleeding possible during surgery). Biopsy is contraindicated
- M/c presentation – recurrent epistaxis and progressive nasal obstruction may be present – *frog face deformity*, proptosis may be present
- On posterior rhinoscopy – it appears as a pink fleshy mass
- There is involvement of CN 2, 3, 4 & 6
- Investigation of choice – **CECT**. *Antral sign* on CT or *Hollman Miller sign* (anterior bowing of posterior wall of maxillary sinus) is pathognomic of angiofibroma.
- T/t
 - **Surgical excision is TOC**
 - Commonly trans-palatine approach (Wilson's)
 - Extended lat. rhinotomy approach for complete clearance of extra-pharyngeal extensions.
 - RT if intracranial extension found
- Methods of reducing blood loss in angiofibroma
 - Pre-operative: Embolization/ estrogen Rx/ RT/Flutamide Rx.
 - Hypotensive anaesthesia.

Nasopharyngeal Carcinoma

- Squamous cell variety is commonest.
- M/c it arise from lateral wall of nasopharynx (mostly in *supratonsillar fossa of Rosenmüller*)
- Bimodal age peak (common in 5th-7th decades but can

occur in 2/3rd decade). M>F

- A/w early antigens of EBV, HLA2 & 8, chimney smokers, wood and leather worker. Common in China.
- Chemicals like **nickel**, dust from chromium, isopropyl oil, formaldehyde, asbestos can irritate the lining of the nose & predispose to nasal cancer.
- By the time diagnosis is established 70% of patient have enlarged cervical nodes. M/c presentation is cervical lymphadenopathy. Rhinolalia clausa is seen.
- M/c nerve involved is abducent 6 > 5th & 3rd nv. Can involve any CN except 7th & 8th.
- **Trotter's triad / Sinus of Morgagni syndrome** : Conductive deafness + facial pain + ipsi/L palatal paralysis
- Cervical metastasis to jugulodigastric LN or post digastric nodes.
- CT is diagnostic
- **Radiotherapy** is TOC. RND is reserved for persisting nodes when primary has been controlled.

- Wood workers (furniture industry workers) are prone to adenocarcinoma of paranasal sinuses esp. ethmoid sinus.
- Workers in shoe making /Leather industry are prone to cancer of nasal cavity.
- Workers in nickel industry are prone to squamous cell carcinoma of nose (Nasopharyngeal carcinoma).
- Chimney sweepers are at increased risk of SqCC of scrotum, lung & esophagus.

RHINITIS

- Atrophic rhinitis: Also k/as ozena. Young's operation is done.
- Important rhinitis-

	Vasomotor Rhinitis	Rhinitis sicca	Rhinitis medicamentosa
Cause	Parasymp. mediated psychosomatic disorder	Crusting due to hot, dry, dusty, surrounding	Long term use of antihistaminics/ decongestant nasal drops
CI/F	Nasal obstruction, excessive rhinorrhea	Crusting	Blockade of nose
T/t	Vidian neurectomy	Nasal irrigation with application of oil	Discontinuation of precipitating drug Submucosal diathermy of inf. turbinate

PHARYNX & ORAL CAVITY

- *Cancrum oris (Noma)* is a fulminant gangrenous infection in children seen after chronic debilitating illness (e.g. Measles) malnutrition, scarlet fever, TB, immuno deficiency. Starts as necrotic ulcer in gingiva of mandible. D/to Fusobacterium nucleatum, pseudomonas. T/t is high dose penicillin.
- *Gingivitis* is infection of gums d/to Gm⁻ anaerobic rod Prevotella intermedia.
- *Herpangina* is caused by coxsackie virus. There is sore-throat, fever, myalgia, vesicular enanthem on palate.

Lateral pharyngeal space Vs.

Retropharyngeal space infection

Lat. pharyngeal space infection (Parapharyngeal/ Pharyngomaxillary space)	Retropharyngeal space infection (Space of Gillette)
<ul style="list-style-type: none"> • Extends from hyoid bone to base of skull • Infection of posterior (retro-styloid) portion of this space causes swelling of lateral pharyngeal wall which bulges medially. • Infection of anterior portion of space causes medial <u>displacement of tonsil</u>, swelling over parotid, and trismus. 	<ul style="list-style-type: none"> • Lies between pharynx & prevertebral fascia (in front of prevertebral fascia). • Extends from base of skull to mediastinum • May follow trauma, cervical osteomyelitis • Symptoms may be pain in swallowing (dysphagia), breathing difficulty • Hot potato voice. • Seen one side of midline.

VINCENT'S ANGINA Vs. LUDWIG'S ANGINA

Vincent's angina	Ludwig's angina
<ul style="list-style-type: none"> • Also k/as <i>acute necrotizing ulcerative gingivitis / Trench Mouth</i> • Halitosis and ulceration of the interdental papillae. • Cause - <i>Oral anaerobes</i> (P. intermedia) - Gm⁻ fusiform bacilli (<i>Fusobacterium nucleatum</i>) - Spirochete denticola • Patch (grayish-white pseudomembrane) in mouth Tracheostomy in case of glottic edema penicillin (high doses) + metro IV therapy. 	<ul style="list-style-type: none"> • Usually starts in infected Lower Molar 2nd & 3rd. (Cellulitis of floor of mouth) • Rapidly spreading, Life-threatening cellulitis of sublingual/submand spaces. • Cause: Anaerobes, strepto • T/t :- Intubation/emergency

Tonsillectomy

Absolute Indications	Relative Indications	Contraindications
<ul style="list-style-type: none"> Recurrent attacks of tonsillitis Quinsy Tonsillitis causing upper airway obstruction (sleep apnoea) Suspected malignancy 	<ul style="list-style-type: none"> Diphtheria carriers who do not respond to antibiotics Streptococcal carriers Chronic tonsillitis with halitosis Recurrent streptococcal tonsillitis in a patient with valvular heart diseases 	<ul style="list-style-type: none"> Hb <10 gm% Acute URI (even acute tonsillitis) Cleft palate Bleeding disorder Children <3 yr DM, HTN, asthma (uncontrolled, systemic disorder) Epidemic of polio, Menstruation

- H'aige a/w tonsillectomy m/c occurs from paratonsillar plexus of veins.
 - Primary hemorrhage occurs during surgery.
 - Reactionary hemorrhage occurs within 24 hours – combined by clot removal or slipping of ligature
 - Secondary hemorrhage occurs between 6-10 post-op days; m/c cause is infection

QUINSY (peritonsillar abscess)

- Abscess formation in peritonsillar space (b/w tonsillar capsule and sup. constrictor muscle covered by pharyngobasilar fascia).
- Mixed anaerobic infection
- Etiology – recurrent attacks of tonsillitis, obliterate intra-tonsillar cleft (crypta magna)
- CI/F – U/L severe sore throat with high fever
 - Speech is thick and muffled (**hot potato voice**)
 - Odynophagia
 - Uvula is oedematous and pushed to opposite side
- T/t – I&D by Hilton's method

→ Retropharyngeal space is also k/as space of Gillette it is potential site for pyogenic abscess and posteriorly tubercular cold abscess.

→ Node of Roviére is situated in retropharyngeal space.

→ Parapharyngeal abscess is abscess of pharyngomaxillary space.

→ In Quinsy tonsillectomy is done 4-6 weeks after treatment of an abscess (in children). In adults 2nd attack of quinsy forms the absolute indication.

ESOPHAGUS

Dysphagia D/d

- Progressive dysphagia lasting weeks to months esp. in elderly males
Solids > liquids ----- is d/ to ca-esophagus
- Non-progressive dysphagia in middle aged females
Liquids > solids ----- is d/ to cardio-spasm/ achalasia
- Episodic dysphagia to solids lasting several years---Seen in lower esophageal rings
- Dysphagia + chest pain (prolonged h/o heart burn) is seen in --- Reflux esophagitis and stricture

→ M/c esophageal motility disorder is nut cracker esophagus

→ Nut cracker esophagus is seen in esophageal cardiospasm

→ Cork screw/Rosary esophagus is seen in diffuse esophageal spasm.

→ Esophageal injury is m/c in --- Cervical portion.

→ Megaesophagus is seen in --- Chaga's d/s & Achalasia cardia.

→ Hypermotility of esophagus is seen in --- Hypertensive peristalsis.

ACHALASIA CARDIA (Megaesophagus)

- Motor disorder of esophageal smooth muscles in which LES does not relax normally with the swallowing.
- Achalasia cardia is d/ to selective loss of inhibitory neurons in the lower oesophagus. The physiological abnormalities are a non-relaxing LOS and absent peristalsis in the body of oesophagus.
- Inhibitory neurons containing VIP and NO synthase are predominantly involved
- CI/f: Dysphagia both to solid and liquid, pain regurgitation during night.
- D/g:
 - Barium radiology shows 'bird's beak' appearance due to abnormal stricture in the distal oesophagus.
 - Oesophageal manometry shows increased LOS tone, but is often normal.
- T/t: Pneumatic dilatation, Heller's myotomy, Botulinum toxin, Drugs such as CCB's, nitrates, sildenafil
- Heller's extramucosal myotomy of LES is surgical t/t. Now a days laparoscopic myotomy is the procedure of choice.

LARYNX

Common facts : Larynx

- Narrowest part of larynx in adult is --- glottis (crieoid/ sub-glottis in ehild)
[Mnemonic : Crieoid in ghild & Glottis in Gentleman].
- Lymphatic spread is not seen in carcinoma glottis because there is no lymphatic drainage of the glottis
- Main function of larynx--- protection of airway
- Posterior crieo-arytenoid is the only abductor of Lx (s/by RLN).
- Pyriform fossa is present in laryngo-pharynx.

Laryngomalacia

- M/c cause of stridor in newborn ehild.
- M/c congenital condition of larynx.
- Stridor is present but ery is normal . Stridor is d/to partial or complete collapse of supraglottic structures on inspiration
- Stridor is intermittent i.e. ↑ ed ed on crying and relieved in prone position.
- 'Omega shaped' epiglottis seen.
- T/t: Wait and watch. Rarely aryepiglottoplasty or supraglottoplasty may be required

→ Cry is normal in → Laryngomalacia, subglottic stenosis, & congenital subglottic hemangioma.

→ Cry is abnormal in → Laryngeal web, laryngeal paralysis, congenital laryngeal cyst. (VC are abnormal)

Laryngocoele

- It is air filled cystic swelling due to abnormal dilatation of the sacule of the ventricle.
- Laryngocoele arise from raised transglottic pressure as in trumpet player, glass blowers.
- Presents as hoarseness, cough, airway obstruction.
- External laryngocoele pierces thyrohyoid membrane.
- D/g can be made by laryngoscopy. Soft tissue X-ray.
- T/t is surgical excision through an external neck incision. Marsupialization of an internal laryngocoele.

Laryngeal Pseudo-sulcus

- Infraglottic edema extending from the anterior commissure to the posterior larynx.
- Seen on ventral surface of vocal fold, in laryngo-pharyngeal reflux
- Also called pseudosuleus-vocalis

Zenker's Diverticulum

- Also k/ as pharyngo-esophageal diverticulum
- Outpouching of anterior pharyngeal mucosa d/to defect in cricopharyngeus, lies just above this m/s
- Occlusive mechanism is most important factor. ZD is a pulsion diverticulum caused by high pressure proximal to LES & UES (Recall that mid esophageal diverticulum is a traction diverticulum).
- Symptoms are oropharyngeal dysphagia & regurgitation of undigested food → foul smelling odor from mouth.
- Simple barium swallow is sufficient to diagnose.
- Endoscopy is contraindicated (risk of perforation).
- T/t: No t/t for asymptomatic/ small Z~, for large symptomatic cases incise cricopharyngeus.

Killian's dehiscence

- Herniation or outpouching of posterior pharyngeal mucosa, through Killian's Laimer triangle, just above esophagus.
- Inferior constrictor m/s has 2 parts - thyropharyngeus (oblique fibres) and cricopharyngeus (transverse fibres) the potential space b/n fibres is known as k~. It is vulnerable for perforation during esophagoscopy.

Passavant's ridge ---

Is formed by contraction of palatopharyngeus & superior constrictors. Soft palate makes firm contact with it during deglutition or speech & cut off nasopharynx from oropharynx

Androphonia is male voice (low pitch) in females. Corrected by type IV thyroplasty (lengthening of VC)

Puberphonia (Adolescent/mutational falsetto) is persistence of high pitch voice usually in males beyond the age at which the pitch of ones voice is expected to lower. T/t is type III thyroplasty (shortening/loosening of VC) for extreme cases.

→ *Puberty dysphonia* is due to --- Over tensed vocal cords

→ *Functional aphonia or hysterical aphonia* --- A functional disorder seen in emotionally labile females

→ *Dysphonia plica ventricularis* --- voice is produced by ventricular bands / false vocal cords.

→ *Spasmodic dysphonia (Laryngeal dystonia)* is d/ to --- Psychological or neurological cause.

→ *Neoglottis phonatoria* --- Post-laryngectomy neoglottis reconstruction

→ After total laryngectomy esophageal speech is utilized in voice production.

→ Topical mitomycin -C , antibiotic isolated from streptomycetes *caepitosus* is used for t/t of laryngeal stenosis.

Spasmodic dysphonia (Laryngeal dystonia)

- Spasmodic dysphonia is used to describe a neurological condition that results in involuntary movements of the vocal folds. There are two types:
Adductor type – Voice sounding strained /strangled
Abductor type – Voice having uncontrolled bursts of breathness or involuntary voice breaks.
- The exact cause is still debated. Most people believe it has either a psychological (following a traumatic event) or neurological (due to abnormalities in the brain) origin
- M/c t/t is intra-laryngeal injection of botulinum toxin. May require monthly injections.

Croup

(Acute Laryngotracheobronchitis, ALTB)

- Affects children 3 months to 3 year esp males.
- Mainly d/to *parainfluenza virus (type 1 & 2)*; also d/to RSV, influenza virus, mycoplasma
- M/c symptom : **Cough**
- CI/f: Fever, hoarseness of voice, seal bark cough, inspiratory or biphasic stridor
- X-ray (AP-view) :- Sub- glottic edema (*Hourglass sign*) & *steeple sign* / pencil tip sign on PA view

Acute Epiglottitis

- Caused by **Hib** (*Haemophilus influenzae type b*).
- M/c symptom : Dysphonia & stridor (cough is not seen).
- CI/f : 2-7 yrs children (male > female) present with high fever, inspiratory stridor. Baby sit in tripod position.
- Onset is abrupt & progression is rapid, child may die in a day.
- Lateral X-ray neck :- Enlarged epiglottis (*Thumb sign*)
- T/t :- Emergency hospitalization and airway management.

Recurrent Laryngeal Papillomatosis

- Benign lesion of larynx and trachea usually seen in children.
- Lesions are multiple & known for recurrence.
- Caused by HPV 6 and 11
- Warts are formed on larynx
- CI/f : Stridor is inspiratory initially but later it becomes biphasic. Airway obstruction worsens as the papilloma grow
- All children with stable obstruction should undergo flexible fibreoptic nasopharyngoscopy by specialist.

- IFN α (Interferon alpha) c/b used in t/t of juvenile laryngeal papillomatosis.
- T/t to prevent recurrence. : Endoscopic removal with cup forceps, cryo, micro-electro-cautery and CO2 laser are preferred.

Vocal nodules

- Also k/ as **singer's or screamer's nodes**
- Small, solid, benign, *non-neoplastic* lesions of larynx
- They appear **bilaterally symmetrically** on the free edge of VC, **at the junction of anterior 1/3rd with post 2/3rd of VC** as this is the area of maximum vibration of VC and thus subjected to maximum trauma
- Vocal abuse / vocal trauma is the cause, when person speaks in low tones for prolonged period or at high intensity
- CI/f – hoarseness is chief complaint
- T/t : **Speech therapy is TOC**
 - Conservatively by *voice rest* (in early stages)
 - Microlaryngoscopic excision (for larger / prolonged nodes)

D/d of solid non-neoplastic lesions of larynx

Lesion	M/c cause	Site	T/t
1. <i>Vocal nodules</i> (singer's /	Vocal abuse	M/c site is junction of anterior 1/3rd + post. 2/3rd VC (B/L)	- Voice rest - Microlaryngoscopic excision for large nodules
2. <i>Vocal polyps</i> (u/L)	Vocal abuse	Junction of anterior 1/3 rd + posterior 2/3 rd of VC (B/L) but +/- U/L	- Surgery (microlaryngoscopic removal)
3. <i>Reinke's edema</i> (B/L diffuse polypoid)	Vocal abuse, smoking	Subepithelial space of Reinke	- VC stripping

- *Vocal polyps can also result from vocal abuse and treated in same way as nodules, but they are usually unilateral at the same position*
- *Reinke's edema (bilateral diffuse polypoid) is d/to vocal abuse (hoarseness) and smoking. Submucosal loose CT layer of vocal cords. Treated by VC stripping/decontamination.*
- In indirect laryngoscopy anterior commissure is difficult to visualize
- *Direct bronchoscopy can visualize --- Trachea, VC, but can not visualise subcarinal LN*

Contact ulcer / Kiss ulcer

- Change in voice d/to voice abuse.
- M/c site is posterior arytenoid
- T/t : speech therapy

Intubation granuloma

- M/c site is junction of anterior 2/3rd + posterior 1/3rd.
- TOC is laser surgery + voice rest.

- Vocal polyps (or vocal nodules) are seen at the junction of anterior 1/3rd + posterior 2/3rd of VC.
- Intubation granulomas are seen at the junction of anterior 2/3rd + posterior 1/3rd of VC.
- Pachydermia laryngis is seen at posterior portion of VC. There is thickening of epithelium in the region of arytenoid

Laryngo-pharyngeal Reflux (LPR) can cause :

- Pachydermia laryngis
- Pseudosulcus vocalis
- Acquired sub-glottic stenosis

CARCINOMA LARYNX/ GLOTTIS

Type	Supra/G	Glottic	Sub/G	Trans/G
Confined to	Ant 2/3rd of VC			Involves paraglottic space
VC	Mobile	Usually mobile		Usually fixed
Earliest symptom	Pain/ feeling of mass	Hoarseness	Resp. difficulty	Hoarseness
Metastasis	To cervical LN	very rare & late		Lymphatic spread
T/t	RT	RT/Sx	Sx	Sx/RT

- SqCC is the m/c type of laryngeal cancer
- ↑ incidence in males, smokers, and alcoholics.
- M/c symptom of laryngeal cancer ---- hoarseness
- M/c site for laryngeal cancer ---- supra glottic area above false vocal cords.
- Ca in situ of vocal cords (CIS-VC)
Often discovered following multiple strippings of VC for leukoplakia, atypia, dysplasia. TOC is stripping +full course of radiation.
- Infraglottic Ca. :
Commonly spreads to mediastinal LN.
- Stages

T₁ : Tumour in only one part of the larynx

T₂ : Tumour in >1 part of the larynx +/- VC involvement

T₃ : If tumour made vocal cords fixed.

T₄ : If tumour invades thyroid cartilage

- T/t for Ca larynx early lesion <2 mm-radiation & >2 mm radiation + surgery
- T/t of Ca Larynx
T₁ and T₂ with N₀ → Radiotherapy (RT) is TOC
T₃ and T₄ with N₀ → Surgery f/b RT
Any T with
+ve neck nodes (N₊) → Surgery f/b RT
T₁ glottic cancer → Best treated by Endoscopic laser cordectomy
T₃ N₀ M₀ with stridor → Tracheostomy
For surface lesion → R_T
Small lesion fixed VC → R_T
Large lesion fixed VC → Total Laryngectomy.
- Horizontal partial laryngectomy is done in T₂ supraglottic cancer while vertical partial laryngectomy is done in T₂ glottic cancer .
- There is no role of chemotherapy.

Site of Larynx affected in

D/s	Part of larynx most affected	Other/f
1. TB	Post > ant (posterior commissure)	<ul style="list-style-type: none"> ◦ Mouse nibbled VC ◦ Turban epiglottis ◦ Tongue is m/e site in oral cavity ◦ TB larynx is painful
2. Lupus vulgaris	Anterior	<ul style="list-style-type: none"> ◦ Apple jelly nodules on nose ◦ Painless
3. Syphilis	Any part of Lx Ant. 1/2 of glottis	<ul style="list-style-type: none"> ◦ Serpiginous ulcer on epiglottis
4. Leprosy	Stenosis of larynx	
5. Cancer Lx	Anteriorly	

[Remember that in TB posterior part of scrotum affected more while in syphilis anterior part of scrotum is affected more]

Keratosis of Larynx

- VC are normally lined by stratified squamous epithelium
- ↑ Rate of keratinisation is seen in smokers and it leads to keratosis of larynx.
- T/t : Quit smoking, cordectomy, decortication of VCs.

Laryngeal Nerve Lesions

Superior LN (Ext LN + Internal LN)

ELN supplies cricothyroid m/s (which is adductor & tensor. Tensors including vocalis gives quality to voice. So in SLN lesion voice is weak & husky, loss of timber (poor quality voice not suitable in singing). ILN is sensory to larynx above VC. So a lesion of ILN causes aspiration pneumonia and death.

RLN : U/L complete section

Speech is not affected much. VC in half abducted position or sometimes called cadaveric position.

RLN : U/L partial section

VC is in adducted (midline) position of affected side.

RLN : B/L complete section

Both VC are in midway b/n abducⁿ & adducⁿ breathing is impaired since rima glottidis is partially closed.

RLN : B/L partial section

Acute breathlessness - dyspnoea & stridor. Both VC are adducted (B/L abductor palsy). Emergency cricothyroidotomy or tracheostomy is necessary.

• **Abductor paralysis** — VC midline, normal voice but respiratory difficulty; tracheostomy required in b/L cases

• **Adductor paralysis** — VC lateral, change in voice but no respiratory difficulty, prone for aspiration.

• **B/L Abductor paralysis** --- Treated by tracheostomy, arytenoidectomy, or cordectomy. TOC is VC lateralisation (type II thyroplasty)

• **B/L Adductor paralysis** — TOC is VC medialisation (type I thyroplasty). Injection of teflon in VC is also effective.

• **Adductor spasm** --- Strained and cracky voice with spasmodic dysfunction

→ Bronchial carcinoma m/c involves --- RLN

→ M/c nerve injured during thyroid surgery --- RLN (right sided)

→ Overall left RLN injury is more common

→ BOTOX injection in PCA (posterior crico-arytenoid) should be reserved for abductor spasmodic dysphonia

Vocal cords (VC)

• Cadaveric position of VC is seen in --- u/L or b/L complete paralysis of RLN + Sup LN

• Most dangerous position of vocal cords --- B/L abductor palsy.

• M/c cause of vocal cord paralysis --- injury to the recurrent LN during thyroidectomy

• M/c sign of unilateral vocal cord paralysis --- hoarseness

• M/c sign of bilateral vocal cord paralysis --- stridor

• Mc benign tumour of vocal cords --- squamous papillomas (a/w HPV 6 & 11)

Thyroplasty (Ishiki Classification)

Type 1 : It is medial displacement of VC (achieved by teflon paste injection)

Type 2 : It is lateralization of VC to improve airway

Type 3 : It is used to shorten (relax) the VC

Type 4 : To lengthen/ tighten or to make VC tense and ↑ es pitch. If converts male character of voice to female

(Mnemonic to remember MSL from 1 to 4)

Rehabilitation after total Laryngectomy.

• Requires developing new voice using Esophageal speech (Using pharyngo-esophageal junction during inspiration) & by creating tracheo-esophageal fistula (expiratory voice).

Blom Singer Prosthesis

Is a variety of TEP (tracheo-esophageal puncture) device. It is used for vocal rehabilitation of laryngectomised patient. (Electrolarynx).

Phonesthesia

• Laryngeal m/s tired or fatigued. T/t is voice rest

• Normally two m/s --- interarytenoid or thyroarytenoid are involved

- If thyroarytenoid is involved --- spindle shape

- If both m/s are involved --- 'key hole' appearance

FACIAL NERVE LESIONS

Topo diagnostic tests

Are used to localize the site of facial nerve lesions and include

• Schirmer's test -- It compares lacrimation of 2 sides.

• Stapedial reflex -- tested by tympanometry

• Submandibular salivary flow test

• Taste test -- by electrogustometry

Electro diagnostic tests

• Conduction and condition of muscles supplied.

- Nerve-excitability test, Electro neuronography
- Strength – duration curve

Site of lesion	Effect
1. A lesion at the stylomastoid foramen	Paralyses all muscles of facial expression
2. In the facial/middle ear canal	<i>Chorda tympani</i> is damaged and in addition to (A) the taste sensation from the anterior 2/3rd of the tongue is lost on the same side.
3. A higher lesion in the facial canal	Results in additional hyperacusis as the nerve to the stapedius is paralyzed
4. At the geniculate ganglion	<u>lacrimation and salivation are reduced</u> . Here the 8th nerve may also be involved because of its proximity.
5. In the pons	usually the 6th nerve is also involved and there are cont/L pyramidal signs - <i>Millard-Gubler syndrome</i> .
6. In supranuclear facial paralysis	the upper half of the face is less involved as it has B/L innervation. Voluntary movements are involved more than emotional expressions and there are ipsi/L pyramidal signs (UMN type)

Bell's Palsy

- Bell's palsy is the **m/c** cause of idiopathic u/L facial nerve paralysis
- **T/t**:
 - Usually spontaneous recovery.
 - Prednisolone is the **DOC**. if patient reports within 1 week

tab prednisolone is advised 1mg/kg/day for 5 days

→If recovery starts, dose is tapered for next 5 days

→If no recovery or paralysis is complete, same dose is repeated for next 10 days then tapered

- Prednisolone is combined with acyclovir for herpes zoster oticus

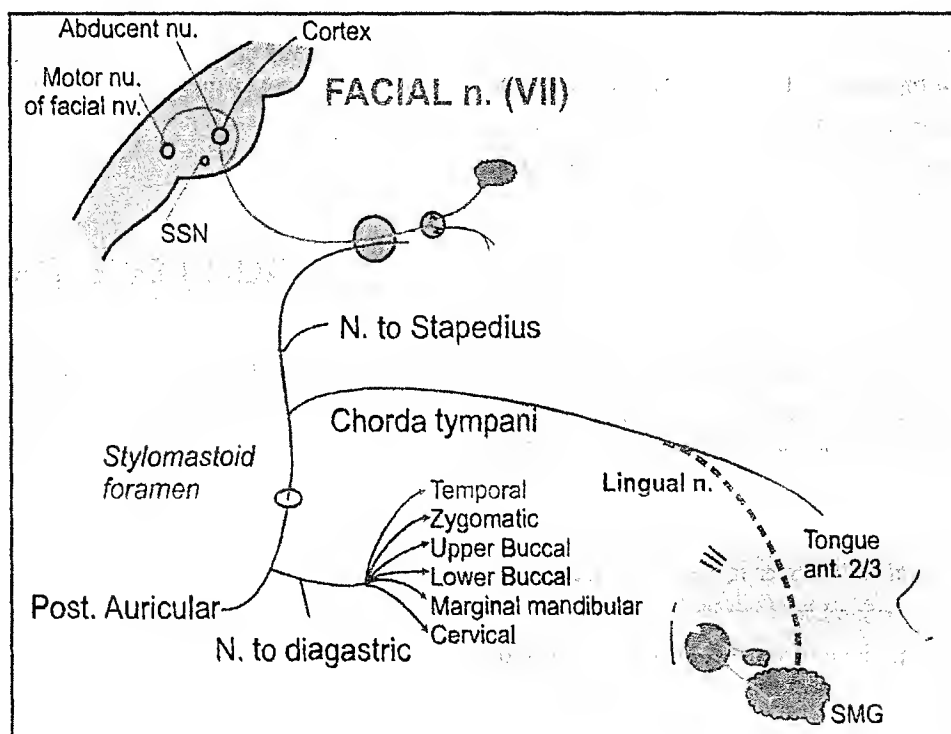
- Prognosis is good . Recovery is complete in 85- 90% of cases

D/d of Facial Palsy

- B/L facial nerve paralysis is seen in sarcoidosis, GBS
- Recurrent facial nerve paralysis is seen in **Melkersson Rosenthal syndrome**. It consists of facial paralysis + swelling of lips + fissured tongue
- Vertical segment of facial nerve is damaged m/c by surgeons . Second m/c site is genu area.

Neonatal facial palsy is seen in

- Mobius syndrome (CN agenesis 6& 7)
- Melkersson Rosenthal syndrome (N~ + face edema + fissured tongue)
- Myotonia dystrophica
- Alberg Schoenberg d/s
- CHARGE association
- Oculo-auriculo-vertebral syndrome



Bilateral facial nerve paralysis is seen in

- Sarcoidosis (M/c cause)
- DM
- Lyme's d/s
- IM
- GBS

Ramsay Hunt syndrome/ Herpes zoster oticus

- Facial palsy + vesicular eruptions/rashes in EAC, pinna and sometimes in pharynx
- CN 7 + 5 (geniculate ganglion) may be affected
- Prognosis is poor (complete recovery only in 10% of cases)
- T/t : Prednisolone and acyclovir

→ Danger area of face is --- Upper lip + lower end of septum + vestibule

→ Danger area of nose is --- Olfactory area

of Temporal bone

- 2 types of # are there :
 1. Longitudinal # (80%)
 2. Transverse # (20%)
- Transverse # results from frontal & occipital blow to head. More likely to cause injury to labyrinth and is more dangerous. Facial nerve palsy is m/c.

SOME IMP INDICATIONS

- **Cortical mastoidectomy** (Schwartz operation)
 - Acute mastoiditis (with coalescence of air cells)
 - Masked mastoiditis (mastoid reservoir phenomena)
- **Radical mastoidectomy**
 - Indication: Unsafe CSOM with extensive d/s, cholesteatoma, glomus tumour & Ca middle ear
 - All of the middle ear structures are removed except stapes. In end eustachian tube is plugged with cartilage.
 - Not indicated in children < 12 yr.
- **Modified Radical Mastoidectomy (MRM)**
 - Indication : Unsafe CSOM + atticoantral d/s or hearing loss or facial nerve palsy or vertigo or labyrinthine fistula (+ve fistula sign).
 - Only diseased ossicles are removed.

- **Tympanoplasty**
 - Cholesteatomas mastoiditis without complication
- **Stapedectomy**
 - Otosclerosis with good A-B gap and good cochlear reserve
- **Myringotomy**
 - ASOM with bulged TM on the point of rupture
 - Unresolved AOM
- **Myringoplasty**
 - Dry central perforation without mastoid pathology and intact ossicular chain
- **Laryngopharyngectomy**
 - Usually accompanied with block dissection of the neck in
 - Pyriform fossa cancer (Inferior hypopharyngeal cancer)
 - Post-cricoid cancer
 - Failed radiotherapy in hypopharyngeal cancer

POINTS OF SPECIAL MENTION

• Ototoxic Drugs

1. Aminoglycosides (Amika/ Genta)
2. Anticancer (Cisplatin)
3. β -blockers (Propranolol)
4. Chelating agents (Desferroxamine)
5. Diuretics (Furosemide)
6. NSAIDs (Salicylates/aspirin, ibuprofen, indomethacin)
7. Quinine/Chloroquine

Ototoxicity is classically reversible with aspirin.

• Radiological Signs in ENT

	Imaging method	Seen in /Condition
◦ Thumb sign	X-ray soft tissue neck (lateral)	Acute epiglottitis
◦ Steeple sign/ (Hourglass/ pencil tip sign)	X-ray soft tissue neck (lateral)	Acute LTB
◦ Phelps's sign	CT	Glomus jugulare
◦ Delta sign	CT	Sigmoid sinus thrombosis
◦ Antral sign (Holman Miller sign)	CECT	Nasopharyngeal angiofibroma
◦ Dodd's sign	X-ray	Nasopharyngeal angiofibroma
◦ Lyre's sign	MRI	Carotid body tumour
◦ Tear drop opacity	X-ray	Blow out # of orbital floor

Site of Origin

Pathology	Seen in /Location
○ Acoustic neuroma	Superior vestibular division of 8th CN
○ Nasopharyngeal Ca	Fossa of Rosenmuller
○ Angiofibroma of nose	Sphenopalatine foramen
○ Inverted papilloma	Lateral wall of nose
○ Esthesio-neuroblastoma (Olfactory neuroblastoma)	Olfactory neuroepithelium

Epiglottitis

Finding	Seen in
Thumb sign	Acute epiglottitis
Serpiginous ulcer	In Syphilis
Omega shaped epiglottitis	In laryngomalacia
Turban epiglottitis	TB Larynx

Trotter's triad

Is seen in carcinoma nasopharynx.

1. Pain on the ipsi/L side of face due to 5th nv. involvement (trigeminal neuralgia)
2. Conductive deafness
3. Palatal palsy / fixation.

Gradenigo's syndrome -

Triad of

- Apex of petrous/ petrositis
- Vth CN involvement (retro-orbital pain)
- VIth CN involvement (Lat rectus with diplopia)

Gradenigo's syndrome (GS) was first described by Giuseppe Gradenigo in 1904 when he reported a triad of symptoms consisting of periorbital unilateral pain related to trigeminal nerve involvement, diplopia due to sixth nerve palsy and persistent otorrhea, a/w bacterial otitis media with apex involvement of the petrous part of the temporal bone (petrositis).

Melkersson's syndrome -

Triad of

- Recurrent facial palsy
- Swelling of lips
- Fissured tongue

Vander Hoeve's syndrome -

Blue sclera + Otosclerosis + Osteogenesis imperfecta.

Blue eardrum is seen in

Hemotympanum (as in temporal bone fracture), glue ear, glomus tumour & hemangioma of middle ear.

Prussak's pouch :

- The inferior pouch of outer attic of middle ear.
- The inflammatory exudates in P~ often leads to perforation of the pars flaccida.

Lever ratio

Between the handle of malleus and the long process of incus is 1.3:1.

Hennebert's sign

Is a positive fistula sign in absence of fistula. (it is seen in congenital Syphilis due to excessively mobile stapes). +ve in 30% of Meniere's d/s patients

Krause's nodes

Are LN situated in jugular foramen. Enlargement of these nodes causes *jugular foramen syndrome* by compression effect on CN 9,10, & 11

Montgomery's T tube

Silicon tracheal tube used for surgical m/m of tracheal stenosis.

Node of Roviore

Is the most superficial LN of the lateral gp of retropharyngeal space.

Reinke's space

Often affected by edema k/as Reinke's edema & causes polypoid degeneration of vocal cords.

Turban epiglottitis

Edema & infiltration of the epiglottis caused by TB larynx

Omega shaped epiglottitis

Is seen in laryngomalacia

Mouse -nibbled VC are seen in TB

Structures of ear fully developed at birth

Middle ear, malleus, incus, stapes, labyrinth & cochlea

[MIS MLC]

Fluctuating hearing loss is seen in ---

Serous OM (otitis media with effusion)

Ménière's ds,

- Perilymph fistula,
- Malingering
- ❑ Commonest site of involvement in stapedial otosclerosis is located at the anterior edge of oval window in the area of fistula ante fenestrum
- ❑ Carhart's notch is b/c of loss of bone conduction & dip at 2000 Hz (in Otosclerosis)
- ❑ Noise induced hearing loss shows a dip at 4000 Hz or above in air conduction curve of audiogram.
- ❑ Acceptable level of noise in industries in India 90 dB for 8 hrs a day for 5 days a week.
- ❑ **Silverstein Microwick microcatheter** sustained release preparation are used to deliver medications (steroids and gentamycin) to round window membrane
- ❑ *Nasolabial cyst*
Soft-tissue lesion developing from **odontoid epithelium** within the labial vestibule just below the attachment of the nasal ala in the maxilla. The clinical presentation is one of upper-lip swelling or of swelling within the floor of the nose. It should be excised from an intraoral approach.
- ❑ M/c site of oral TB --- Tongue
- ❑ Meningitis leads to vestibulitis through cochlear aqueduct.
- ❑ *Hyrtle's fissure* is an embryonic hole that connects hypotympanum to sub-arachnoid space (tympano-meningeal hiatus).
- ❑ Stapes and related structures develop from 2nd arch while stapes foot plate (otic capsule) develops from neuroectoderm.
- ❑ Otoacoustic emissions arise from outer hair cells.
- ❑ Middle superior alveolar nerve is a branch of --- Palatine branch of maxillary nerve.
- ❑ Infection from meninges can transfer to labyrinth through cochlear aqueduct.
- ❑ Endolymph is secreted by stria vascularis.
- ❑ Distance b/w pharyngeal opening of auditory tube and posterior end of inferior turbinate is 31 cm.
- ❑ *Lower CN (9,10,11,12) palsies in ENT*
 1. Glomus jugulare
 2. Malignant otitis externa
 3. Nasopharyngeal carcinoma
- ❑ *ENT conditions common in females*
 1. Glomus jugulare
 2. Atrophic rhinitis
 3. Functional aphonia

4. Post cricoid carcinoma
5. Otosclerosis

❑ *Potentially disfiguring conditions of nose*

1. Leprosy (saddle nose)
2. TB
3. Rhinoscleroma

SOME IMP. NEGATIVE POINTS ASKED IN EXAMS

- ❑ Tracheostomy is NOT indicated in --- Uncomplicated bronchial asthma
- ❑ NOT true about Radical mastoidectomy --- Eustachian tube is excised.
- ❑ About Vincent's angina NOT true --- Can extend into mediastinum.
- ❑ Tympanic cavity does NOT contains --- Posterior auricular nerve.
- ❑ Medial wall of middle ear is NOT formed by --- TM.
- ❑ Rinne's test is NOT negative in --- Normal ear
- ❑ NOT a c/c of tracheostomy --- Rupture of internal jugular vein, Myxedema
- ❑ Membrane on Pharynx is NOT seen with--- Staphylococcus.
- ❑ Nasal septum is formed by --- Lacrimal bones
- ❑ Anterior ethmoidal nerve do NOT supply--- Maxillary sinus.
- ❑ Facial nerve does NOT contain --- Somatic efferents
- ❑ Spontaneous CSF leak is NOT seen in --- Low risk encephalocele.
- ❑ NOT a common cause of nasal septal bleed ---Thrombocytopenia.
- ❑ Labyrinthine dysfunction are NOT seen in --- Vertebro-basilar ischemia.
- ❑ NOT a cause of septal perforation --- Rhinosporodiosis.
- ❑ NOT a cause of conductive deafness --- Endolymphatic hydrops.
- ❑ Trotter's triad does NOT include --- Seizures
- ❑ NOT an extrinsic ligament of larynx --- Hypoepiglottic membrane.
- ❑ Intranasal approach is NOT used for accessing --- Cerebellum

CLINICAL VIGNETTES

A 30 year old male suddenly developed hoarseness, stridor, neck swelling and swelling of the tongue after eating peanuts. The diagnosis is: [AIIMS May'07]

- A. Foreign body bronchus
- B. Foreign body larynx
- C. Parapharyngeal space abscess
- D. Angioneurotic edema

[Ans. : D. Angioneurotic edema]

A 5 year old child suffers recurrent upper respiratory tract infections. She has nasal blockage with mouth breathing and bilateral impairment of hearing. The ideal treatment is: [AIIMS May'07]

- A. Bilateral myringotomy
- B. Bilateral myringotomy and grommet insertion
- C. Adenoidectomy and grommet insertion
- D. Tonsillectomy

[Ans. : C. Adenoidectomy and grommet insertion]

Child is having adenoids (enlarged nasopharyngeal tonsils). There is a typical h/o recurrent URI, nasal obstruction and mouth breathing (adenoid facies). Earache and deafness are associated. If symptoms are marked then it is best treated by adenoidectomy

A case of carcinoma larynx with the involvement of anterior commissure and right vocal cord, developed perichondritis of thyroid cartilage. Which of the following statements is true for the m/m of this case?

- A. He should be given radical radiotherapy as this can cure early tumours
- B. He should be treated with combination of chemotherapy & radiotherapy
- C. He should first receive radiotherapy and if residual tumour is present then should undergo laryngectomy
- D. He should first undergo laryngectomy and then post-operative radiotherapy

[Ans.: D]

Carcinoma larynx which involves anterior commissure, right vocal cord and thyroid cartilage means T4 glottic cancer and it is best treated by total laryngectomy with post-operative radiotherapy

Rajesh, a 7 month old child, presents with failure of gaining weight and noisy breathing which becomes worse on crying. Laryngoscopy shows a redish mass in subglottic area. T/t modalities are A/E [AIPGMEE 2003]

- A. Radiation
- B. Steroids
- C. Tracheostomy
- D. CO₂ laser

[Ans.: A. Radiation]

It is a case of subglottic hemangioma, which is characterized by

- Redish blue subvocal mass which increases in size at the age of 3-6 month
- Stridor worsens on crying
- Resolve spontaneously, other t/t options are tracheostomy, steroid therapy, CO₂ laser excision

A 10 year old child comes to OPD with complaints of less opening of mouth. O/E there were few white bands over hard palate. Most likely d/g is-

[MAMC MO exam 2008]

- A. Aphthous ulcers
- B. Palatal leukoplakia
- C. Submucous fibrosis
- D. Erythroplakia

[Ans. B. Palatal leukoplakia]

A newborn is brought with inspiratory stridor, which was more in supine position and was increasing with feeding. O/E there was omega shaped epiglottis. What will you do [MAMC MO exam 2008]

- A. Urgent admission
- B. IV antibiotics
- C. Systemic steroids
- D. Reassurance to the parents

[Ans. D: Reassurance to the parents]

Neonate is having laryngomalacia, which is a self limiting condition. Reassurance of the parents is required. Stridor usually settles on placing the child prone.

A 50 yr male presents with non-progressive dysphagia predominantly for solids for the past 2 years. Barium swallow showed dilated distal esophagus with terminal narrowing. The most probable diagnosis is :

[AIPGMEE'10]

- A. Achalasia cardia
- B. Carcinoma esophagus distal end
- C. Peptic stricture
- D. Carcinoma fundus of the stomach

(Ans.: A. Achalasia cardia)

- Progressive dysphagia lasting weeks to months esp. in elderly males --- Solids > liquids is d/ to ca-esophagus.
- Non-progressive dysphagia in middle aged females --- liquids > solids is d/ to cardio-spasm/ achalasia.

We are trapped here as the age, sex and dysphagia more for solids are in favour of carcinoma esophagus. But all these can occur in achalasia also. Dilated distal esophagus with terminal narrowing (Bird's beak appearance) is more in favour of achalasia rather than carcinoma.

- Episodic dysphagia to solids lasting several years---Seen in lower esophageal rings
- Dysphagia + chest pain (prolonged h/o heart burn) is seen in --- Reflux esophagitis and stricture.

- CT orbit is required to confirm the lesion and its extent, to resolve discrepancies of symptoms and signs. Nasal endoscopy adds further in diagnosing.

NOTES

- A diabetic elderly male presents with lesion in external ear resistant to antibiotics with facial nerve palsy. Which of the following is likely diagnosis? [AIPGMEE'12]

- (A) Malignant Otitis Externa
- (B) ASOM with complications
- (C) Middle ear malignancy
- (D) Bell's palsy

[Ans. (A) Malignant Otitis Externa]

Malignant otitis externa is caused by *pseudomonas aureginosa*. It is a/w facial nerve palsy.

- A 40 yr old Man presented with chief complains of dysphagia grade 2, fatigability and foul smelling breath since a month. On examination were heard in lungs. Which of the following is most possible diagnosis?

[AIPGMEE 2012]

- (A) Schatzki ring
- (B) Zenker's diverticulum
- (C) Corkscrew esophagus
- (D) Plummer Vinson syndrome

(Ans: (B) Zenker's diverticulum)

Foul smelling breath is because of collection of food in pharynx which is seen in pharyngeal diverticulum. Plummer vinson is common in females.

- A 2½ yr female child presents with swelling around eye with conjunctival discharge. Conjunctival swab is normal. X-ray PNS showed opacity of left ethmoid. Blood picture showed neutrophils 17% increase in lymphocytes. Next line of Ix is: [AIPGMEE'10]

- A. CT orbit
- B. Repeat culture from conjunctival discharge
- C. Blood culture
- D. Urine culture

(Ans.: A. CT orbit)

- Clinically it looks like a c/o chronic rhinosinusitis.

GENERAL ORTHOPAEDICS

Fracture (#) overview

- Most consistent/ pathognomonic sign of a fresh # is ---crepitus (bony tenderness)
- Mechanism of #**
Direct impact on bone will produce a --- Transverse #
Crushing is more likely to cause --- Communitied #
Twisting results in spiral # & compression in oblique #
- A partial or complete loss of continuity of bone is essential for diagnosis of a #
- Stages of # healing ---**
First stage is hematoma formation → soft callus → hard callus → modelling → remodelling is last
- Most important factor in # healing is ---immobilization
- M/c bone fractured in the body is ---clavicle

Imp. causes of pathological

- Osteoporosis is the m/c cause. M/c cause of bone # in India is nutritional → osteoporosis.
- Osteomalacia, hyperparathyroidism, Paget's d/s, osteogenesis imperfecta, multiple myeloma
- Bone cysts, chondroma, osteosarcoma, metastatic bone cancers
- Radiation

→ Pathological # are usually treated by internal fixation

→ Chief mineral of the bone is hydroxyapatite.

Parts of bone

Diaphysis	Metaphysis	Epiphysis
<ul style="list-style-type: none"> Shaft of bone 	<ul style="list-style-type: none"> Area of max^m growth velocity 	<ul style="list-style-type: none"> Growing end
<ul style="list-style-type: none"> Nutrient artery enters a long bone through D ~ 	<ul style="list-style-type: none"> Supplied by "hair pin bends" like end arteries 	
<ul style="list-style-type: none"> TB & syphilis begin in diaphysis 	<ul style="list-style-type: none"> M/c site of osteomyelitis in bone & avascular necrosis 	<ul style="list-style-type: none"> Involved in Perthe's d/s

→ Physeal growth plate (also k/as **growth cartilage**) separates the epiphysis from metaphysis. It is affected in slipped capital femoral epiphysis (SCFE)

→ Structure responsible for longitudinal growth of bone --- Epiphyseal growth plate (physis)

→ Hematogenous infection to bone m/c involves --- Metaphysis of long bones

→ Trevor's disease --- Dysplasia epiphysis hemimelica

Biochemical markers of bone metabolism

	Bone formation	Bone resorption
1. Serum	Bone specific ALP, Osteocalcin (Gla protein), Peptide of type I procollagen	Crosslinked N-telopeptide & C-telopeptide, Serum TRAP, Bone sialoprotein
2. Urine	-	Crosslinked N-telopeptide & C-telopeptide, Total free deoxypyridinoline, Hydroxyproline/ hydroxylysine

→ Substance used for vertebroplasty --- Polymethylmethacrylate (bone cement substance)

→ Bone cement substance commonly used for artificial bone graft --- Hydroxyapatite

→ Substance used for chemonucleolysis (medical discectomy) --- Chymopapain

- Heterotrophic ossification is c/by periarticular (around joints) deposition of ectopic new bone. Serum ALP is an important marker of osteoblastic activity and new bone formation.

- In metastatic calcification serum calcium is most important investigation.

NEUROPRAXIA

Seddon classify nerve injuries into 3 types

Type of injury	Pathology	Degeneration	Tinel's sign	Neuroma	Prognosis
1. Neuropraxia	Only physiological interruption	-	-nt	-	Complete recovery in 6 weeks
2. Axonotmesis	Few axons broken, nerve intact	+	+(advances distally with time)	+(in continuity)	Recovery & motor march+
3. Neurotmesis	All axons + nerve broken	+	+(but will not advance further)	+	Poor nerve repair

- Dislocation and # are m/c cause of nerve injuries
- Post injection nerve palsy is an example of neurotmesis
- Wallerian degeneration is **not** seen in — Neuropraxia
- Leprosy is M/c infection leading to nerve injury. (M/c nerve affected- ulnar nerve)
- Tetracycline injection may cause radial n. palsy.
- Neuronal degeneration may be seen as a part of crush injury, senescence
- In nerve repair ulnar nerve has got the worst & radial n. has the best prognosis.
- Dislocation and # are m/c cause of nerve injuries
- Tinel's sign (Hoffman sign) is seen in Sunderland type 2 & 3 peripheral nerve injuries. It is a distal sign of nerve regeneration.

Signs/Tests

- Kanavels' sign is seen in acute suppurative tenosynovitis of little finger.
- Cozen's test is used to detect tennis elbow.
- Ober's test is used to detect tight iliotibial band.
- Finkelstein's test is used to diagnose DeQuervain's tenosynovitis with wrist pain.
- Tinel's sign, Phalen's wrist flexion test is used to diagnose CTS (Carpal tunnel syndrome)
- Modified Allen's test is used for Radial a.
- Thomas test is used for identifying fixed flexion deformity of the hip.
- Rocker bottom foot is seen in congenital vertical talus & defective correction of CTEV.

Impacted # are commonly seen in

- # Surgical neck of humerus
- # NOF
- # Lower end of radius

Proteins of bone Matrix

Osteoblast derived	Cell adhesion proteins	Osteopodin, fibronectin, thrombospondin
	Ca ⁺⁺ binding	Osteonectin, sialoprotein
	Mineralisation function	Osteocalcin
	Enzymes	Alkaline phosphatases, collagenases
	Growth factor	IGF1, IGFβ, PDGF
	Cytokines	IL-1, IL-6, RNKL
Concentrated from serum		β ₂ microglobulin, Albumin

- Rate of mineralisation of newly formed bone can be estimated by tetracycline labelling.

OR + IF required in

- # in which there are high chances of displacement
 1. # Lateral condyle humerus (Chances of displacement are becoz of common extensor origin)
 2. # Patella (D/to pull of quadriceps femoris)
 3. # Olecranon (D/to pull of triceps)
- Tension band wiring (TBW) is done in transverse # of patella & olecranon, 5th MT

Salter and Harris classification of epiphyseal injuries/ # and t/t in children-

- # Of distal femur (type II) --- OR or CR
- # Medial malleolar epiphysis (Type III)
- # Lateral condyle of humerus (Type-IV)
- # NOF displaced in children
- # Shaft of femur in a child nearing completion of growth

- Type-II epiphyseal injury is commonest

Fracture of Necessity in Children

Fractures in which surgery (operative intervention/ORIF) is must are k/as # of necessity. These are

- # of NOF
- # Lateral condyle humerus
- # Lower end of tibia

Casts/Brace

Cast	Used in
1. Minerva cast, SOMI brace	Cervical spine, # patella
2. Hanging cast/sugar tong cast	# Shaft of humerus
3. Risser's, Milwaukee's	Scoliosis
4. Colle's	# Lower end radius
5. Glass holding	# Scaphoid
6. Boomshek (Petrie's)	Leg Calve Perthe's d/s
7. PTB cast	# Tibia

Splints

- Von Rosen splint --- DDH
- Cock up splint --- Radial n. palsy
- Knuckle bender splint --- Ulnar n. palsy
- Thomas splint --- # femur or # around hip
- Aeroplane splint --- Brachial plexus injury
- Volkmann's splint --- VIC
- Dennis Brown splint --- CTEV
- Crammer wire splint --- Emergency immobilizatⁿ of #

Amputations

In UL

- Ray --- for removal of fingers with metacarpals from CMC joint
- Krukenberg's --- making forceps with two forearm bones

In LL

- Syme's --- through ankle joint
- Boyd's --- amputation below ankle, patient can wear shoes
- Chopart's --- through talonavicular joint
- Lisfranc's --- through intertarsal joints

Length of stumps in various amputations:

Above knee amputation → 12 cm above knee & 18 cm below greater trochanter

Below knee amputation → 15 cm below medial tibial surface

Above elbow amputation → 20 cm from acromion

Below elbow amputation → 18 cm from tip of olecranon

Common Osteotomies

- Mc Murray's --- In # NOF
- Powel's --- OA of Hip, # NOF
- High tibial --- OA of knee
- French --- Correction of cubitus varus
- Spinal/Smith Peterson --- Ankylosing spondylitis
- Wilson's --- Congenital Coxa vara
- Dwyer's --- CTEV
- Salter, Pemberton, Chairi Digas --- in DDH
- Sandwich --- Slipped epiphysis

NAMED FRACTURES

- **Monteggia #** --- # of proximal 1/3 of ulna (medial bone) + dislocatⁿ of head of radius
- **Galeazzi #** --- #/dislocation of distal 1/3 of Radius +/- distal RU joint or ulnar head
- **Colles #** --- # of distal 1/3 rd of radius (within 2-5 cm) with dorsal tilt & lateral, dorsal, and upward (proximal) displacement, supination at corticocancellous juncⁿ.
D/to fall on **outstretched** hand
Dinner fork deformity is seen
T/t:-Cast in hand shake position (ulnar deviation)
- **Smith #** --- Reverse of Colles #, Low radius #, 2-2.5 prox^m to wrist joint (distal end of radius) is involved with *ventral tilt & angulation*
d/to fall on **flexed** hand
T/t :- **above elbow cast**
- **Barton's #** --- # *dislocation of radiocarpal joint* (Marginal #) distal 1/3 of radius fractured with intraarticular communication
Treated by joint - line reduction (to avoid osteoarthritis), JESS
- **Chauffeur's** --- Intra - articular *oblique # of styloid* process of radius. avulsion # in which initial degree of supination/pronation hampered. T/t is always ORIF (with K-wire)

◦ Intraarticular # of base of 1st metacarpal

Bennet's # --- Oblique intra-articular # in boxers d/to fall on outstretched hand a/w subluxation of trapezio-metacarpal joint. R_x -- OR-IF

Rolando's # --- Communitied intra-articular # V-Y #

In Bennett's #, anatomical reduction is difficult to maintain because of dorsal & radial pull of AbPL (abductor pollicis longus) & the adductor further levers the base into abduction.

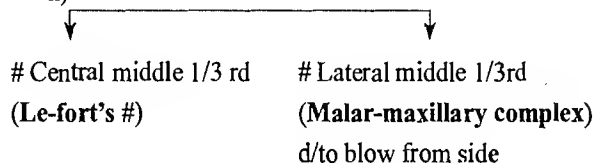
- **Boxer #** --- Vertically displaced # through neck of 5th metacarpal
- **Baby car #** --- # of distal end of humerus with proximal radius / ulna (*Side - swipe injury*)
- **Bumper #** --- Depressed comminuted # of lateral condyle of tibia (causing genu valgum)
- **Pott's #** --- Bimalleolar ankle #
- **Cotton's #** --- Tri-malleolar ankle #
- **Aviator's #** --- # neck of *Talus* (in aircraft injuries)
- **Massonaise #** --- # neck of *fibula*
- **Pilon #** --- # Distal end of *Tibia*
- **Chopart #** --- # dislocation through inter - tarsal joint
- **Jone's #** --- Avulsion # of base of 5th MT
- **March / (Stress #)** --- Fatigue # of shaft of *2nd & 3rd metatarsals*
No # line is seen on X-ray. Pain in metatarsals after long walking / exercise
T/t--- cast immobilization
- **Clay-Shoveler's #** --- Avulsion # of *C₇ / T₁*. Spinous process is fractured
- **Hangman's #** --- # through pedicle & lamina of *C₂* vertebra or subluxation of *C₂* over *C₃*
- Jefferson #** --- # through body of *C₁* vertebra (odontoid view required)
- **Straddle #** --- B/L # of superior & inferior pubic rami. A/w rupture of bulbous urethra and extraperitoneal rupture of bladder

- **Malgaigne's** --- Pelvic # in which there is combination of # (pubic rami anteriorly & sacroiliac / ileum posteriorly on the same side)
- **Dashboard's** --- Results in posterior dislocation of hip
- **Jarjavay's #** --- # of maxillary spine to vomer
- **Chavellot's #** --- # of maxillary spine to root of nose
- **Buckle/Torou's #** --- Occurs near metaphysis in distal forearm in children b/c immature bone is more porous.
- **Night Stick #** --- Isolated transverse # of shaft of ulna (because of stick injury).
- **Green Stick #** --- Seen in children. Cortex is half intact & half bend
(Spontaneous reunion occurs)
- **Crescent #** --- # of Iliac wing with sacroiliac disruption (Pelvic ring injuries with lateral compression force).
- **Stieda #** --- Avulsion injury to the MCL at the medial (internal) femoral condyle.

MAXILLOFACIAL INJURIES & FRACTURES

Middle third of face

(# involving part of face between supra - orbital ridge & upper teeth)



- **Le- forts I / Guerin # / Transverse #**
 - Transverse # through maxilla involving *only palate*
- **Le- forts II / Pyramidal #**
 - # en bloc of the palate & middle 1/3rd of face.
 - Passes obliquely across maxilla may be asymmetrical on both side.
- **Le- forts III (Craniofacial dysjunction)**
 - Most severe type involving complete disruption of attachment of facial skeleton to cranium
 - Passes across root of nose, supra-orbital fissure & zygomatic-frontal sutures

→ *Cribriform plate is injured in Lefort II, III and CSF rhinorrhea may be present.*

Base of Skull

- *Battle's sign* +ve (blood in EAM)
- *Raccoon's sign* (B/L ecchymoses & swelling of upper eyelids) suggest a basal anterior fossa #.
- # of temporal bone (more common) : produces bloody discharge from middle ear (**hemotympanum**) injury to 7th, 8th nerve
- # of sphenoid bone : 3, 4, 6th CN injured
- Streptococcus pneumoniae meningitis common

# Anterior cranial fossa	CSF rhinorrhea Olfactory nerve is m/c involved B/L peri-orbital hematoma (Panda's sign / Raccoon eye sign) Black eye + sub conj. hmg.
# Middle C.F.	CSF otorrhea Duramater is disrupted Nerves injured 6, 7, 8, (Facial nerve palsy +nt)
# Posterior Cranial Fossa	<i>Battle sign</i> (delayed ecchymoses over mastoid) CN involved 9, 10, 11 (but 12th spared)

Floor of orbit

- Diplopia d/to entrapment of extra-ocular muscles.
- Sensory loss over cheek

Zygomatic bone & arch

(# Zygoma / Tripod #)

- D/to heavy and direct blow from lateral side
- C/f: Swelling of cheeks and eyelids, bruising, malocclusion of teeth. *Sub conjunctival hemorrhage present*
- T/t: Elevation + fixation

Blow out # of orbital floor

- Diplopia on looking upward and laterally (d/to trapping of inferior oblique m/s)
- 30° Occipito-mental view X-ray required.
- **Tear drop sign** on antral CT Scan
- T/t --- Elevation + Fixation (Orbital floor exploration, if there is trapping of inferior rectus)

Mandible

- D/to Indirect trauma (blow to chin). B/L in 60% cases
- Commonest site is through neck of condyle (weakest part)

- Masseter muscle's pull on posterior fragment distract the #
- C/f : Hematoma in the floor of mouth if # of body occurs [Coleman's sign]
- R_x : Early reduction + fixation (+Broad spectrum antibiotics in heavy doses)
- Edentulous mandible is immobilized by --- *Gunning's splint*
- *Pre-occlusion view* required for X-rays.

Temporal bone

- Hemotympanum, Battle's sign
- Longitudinal # are m/c (80%) but transverse # are a/w highest chance of facial n. paralysis.

→ *The so called 'motorcyclist's fracture in skull is a --- hinge# which is a basal skull #, transverse crack across floor of skull.*

→ *Ring # around foramen magnum is another skull # which is caused by impact on crown of the head.*

→ *M/c bone #ed in skull - Temporal bone.*

→ *Lefort's # are seen in facio-maxillary trauma.*

COMPLICATION OF FRACTURES

NON- UNION

- M/c cause of non-union is inadequate immobilization
- Causes of non-union are :--- chronic infection, absence of nerve supply, malnutrition, avascular necrosis/ insufficient blood supply
- Very common in # a/w avascular necrosis. E.g.
Head & NOF,
Proximal pole & waist of scaphoid,
Body of talus
- Also seen in
Lateral condyle of humerus,
Lower 1/3rd of tibia/ulna
- D/g usually require at least 9 months post # period (but # NOF is exception in which case non-union c/b labelled after 3 weeks)

Pseudoarthrosis is seen in

- Fractures
- Neurofibromatosis
- Fibrous dysplasia
- Osteogenesis imperfecta
- Congenital

DUPUYTREN'S CONTRACTURE

- Flexion deformity of one or more fingers d/to thickening & shortening of palmar aponeurosis
- Autosomal dominant inheritance has been suggested
- Causes
 - M/c cause is idiopathic
 - Age > 40, male, *smoking*, repeated trauma are *risk factors*
 - A/w --- alcoholism, **diabetes**, epilepsy, cirrhosis, phenytoin therapy, hypoxanthinemia & oxidative stress
 - Peyronie's disease** (*contracture of penis*), Ledder horse disease (contracture of sole/plantar fascia)
- B/L in 45% Cases
- Pathognomonic & earliest lesion - palpable nodular thickening of palmar fascia along pretendinous band
- **Ring finger** is affected most commonly (small hard nodule over head of 4th metacarpal)
- Flexion at MCP & PIP joint (*DIP remains normal*)
- T/t : Partial fasciectomy for palmar d/s. After surgery hand is splinted in position of extended PIP joint.

COMPARTMENT SYNDROME

- Results from ↑ in compartment pressure (from any injury leading to muscle edema, # hematoma or ischemia)
- Necrotic muscles may undergo healing with fibrosis leading to contractures (e.g VIC)
- **Injuries with high risk of developing compartment syndrome & VIC are**
 - Closed tibial # (**m/c** cause)
 - Soft tissue/ crush injuries to leg and forearm
 - Supracondylar # of humerus
 - Forearm bone # [mnemonic: Test C S E]
- Gallow's traction can cause VIC.
- Stretch pain test is the earliest sign of impending compartment syndrome
- T/t early surgical decompression by incision in fascia (*fasciotomy*).

VOLKMAN'S ISCHEMIC CONTRACTURE (VIC)

- M/c sequelae of compartment syndrome/ Volkmann's ischemia. The ischemic muscles are gradually replaced by fibrous tissue with flexion contracture _
- Commonly seen in supracondylar # humerus, in which occlusion of brachial a & ant. interosseus branch results in **ischemic** damage of flexors of forearm (esp FPL, **FDP medial half**).

• C/I

- Marked atrophy of forearm
- Flexion deformity of wrist and fingers (producing +ve Volkman's sign—fingers can be extended at IP joints only when the wrist is flexed)

• T/t

- usually passive stretching + turn-buckle splint.
- Maxpage operation, surgical fasciotomy (with longitudinal incision)

→ Most diagnostic clinical test of compartment syndrome ---stretch pain test.

SUDECK'S OSTEODYSTROPHY

- Colle's # is the **m/c** cause of it in the upper limb.
- Noticed only after cast is removed. Overlying skin is glossy and stretched.
- T/t - Physiotherapy

CARPAL TUNNEL SYNDROME

- Entrapment neuropathy d/to compression of median nerve in carpal tunnel
- Common in females b/w 40-70 years. Attacks are frequent in nights. Pain may be referred proximally to the forearm and arm.
- Common causes are---idiopathic (**M/c** cause), excessive use of wrist (as in *typists*), Acromegaly, Amyloidosis, DM, Hypothyroidism, RA, pregnancy, etc.
[mnemonic: RADHICA-P]

• C/I

- Wasting of thenar muscles (*ape-like hand*) including Ab PB, FPB and OP which are s/ by median nerve
- Paralysis of opponens pollicis results in loss of opposition of thumb & paralysis of index and middle finger lag behind while making the fist.
- Paralysis of Ab PB results in loss of Abduction of thumb.
- Nocturnal paresthesias of thumb, index and middle finger. Trophic changes (dry scaly skin) in long standing cases . Skin areas with sensory loss are warmer d/to arterial vasodilatation
- Skin over the thenar eminence is not affected as n/s from it arises from the forearm br. of median nerve.

• D/g : **Phalen's** test is used for d/g.

• T/t : Usually spontaneous recovery occurs.

Most common complication of -

Colles #	Stiffness of fingers & wrist > Malunion, shoulder stiffness
Supracondylar # of humerus	Malunion (Gunstock/cubitus varus deformity)
# Lateral condyle of humerus	Non-union
Inter trochanteric # of femur	Malunion with shortening (varus with external rotation)
# Clavicle	Malunion, Shoulder stiffness
# NOF	Non union > Avascular necrosis
Scaphoid #	Non-union/ AVN

Some important complications of # -

Non-union	<ul style="list-style-type: none"> # NOF # Scaphoid # Lower 1/3 rd Tibia # Lower 1/3 rd Ulna Lat. condyle humerus (FLUTS)
Mal-union	(# at the ends of a bone) <ul style="list-style-type: none"> Colles # → Dinner fork deformity Supracondylar # of humerus → Gun stock deformity Inter-trochanteric # of femur
Avascular necrosis	<ul style="list-style-type: none"> Head of the femur (# NOF esp. sub-capital) Proximal pole of scaphoid (# through the waist) Body of the talus (# through the neck)

→ Osteonecrosis of femur head is seen in SCD, Goucher's d/s, Cassion's d/s, hemoglobinopathies

→ Sites commonly affected in traumatic osteonecrosis are --- the head of femur, proximal scaphoid, post half of talus.

→ Nonunion is commonly seen in cases in which avascular necrosis is common

Pulled Elbow

- Head of radius rotates & slips out of annular ligament in children

De Quervain's Tenovaginitis / Tenosynovitis

- Involves 1st extensor compartment
- Inflammation of APL & EPB (Abductor Pollicis Longus + Extensor pollicis brevis) tendon which leads to pain & swelling over radial styloid process

- Finkelstein's test for d/g
- More common in thyroid d/s

Mallet finger ("Baseball" or "drop" finger)

- Swan-neck deformity is a frequent c/c of mallet finger characterized by **hyperextension at PIP** and hyperflexion at DIP joint. Acute m~ is splinted in opposite way (mallet splint).

Trigger Finger/Trigger thumb

- Also k/as Stenosing flexor tenosynovitis of PIP joints (locking of digits in flexion).
- D/to tendon sheath constriction at the level of MCP joint, A₁ pulley
- Causes are : DM, local trauma, unaccustomed work, RA

THUMB

- Gamekeeper's thumb is caused by repetitive microtrauma over the thumb → Injury/laxity to UCL (ulnar collateral ligament) of MCP joint of thumb.
- Skier's thumb is caused by non-repetitive /traumatic rupture of UCL (Ulnar collateral ligament).

TOE

- Hammer toe is fixed flexion deformity of an IP joint (interphalangeal) of toe.
- Morton's toefoot is also k/as Lamay toe. C/by Short 1st MT in relation to 2nd MT (brachymeta-tarsia).
- Hallux valgus is lateral deviation of great toe at the MTP metatarsophalangeal joint usually d/to pointed & high heel shoes, RA etc.

→ Swan-neck deformity is hyperextension at PIP and hyperflexion at DIP joint. Seen in RA, spastic states.

→ Buttonhole or Boutonniere deformity is hyperextension of DIP and flexion of PIP joint seen in RA.

→ Tardy ulnar nerve palsy is a delayed c/c of # lateral condyle of humerus & there is cubitus valgus deformity

→ Kanavel's sign is used for diagnosing infectious tenosynovitis

→ Ganglion is m/c soft tissue tumour of hand & wrist. It arises from leakage of synovial fluid from tendon sheath/joint. It is multilocular cystic swelling usually seen on dorsum of hand (over scapholunate ligament)

→ Rupture of EPL tendon is seen in --- Colles #, RA, DeQuervain's synovitis

→ Tarsal tunnel Syndrome is seen in --- RA

CHRONIC BURSITIS & related conditions

- House-maid's knee --- Pre-patellar bursitis
- Clergy-Man's knee --- Infra patellar bursitis
- Breast Stroker's knee --- Bursa under *pes anserinus* (conjoint insertion of sartorius, gracilis, semitendinosus)
- Student /Miners elbow --- Olecranon-bursitis
- Weaver's bottom --- Ischial bursitis
- Tailor's ankle --- Bursitis over **lat. malleolus**
- Bunion --- Bursitis over medial side of great toe
- Baker's Cyst --- Median posterior swelling of popliteal fossa. Synovial herniation d/to RA, OA, TB (Popliteal bursitis)
- Brodie's bursa --- Under *medial head of Gastrocnemius*
- Golfer's elbow --- Medial epicondylitis of humerus
- Tennis elbow --- Lateral epicondylitis of humerus (painful dorsiflexion of wrist)

→ *Brodie's abscess is seen at proximal end of tibia*

→ *Enthesopathy is inflammatory involvement of insertion site of tendons. Causes are --- ankylosing spondylitis in which there is achilles tendon enthesitis, RA, DISH, Forestaire d/s.*

→ *Pigmented villo nodular synovitis affects knee joint.*

→ *Knee joint communicates with the 3 bursae - supra-patellar, popliteal & semimembranous bursa.*

→ *Poncet's d/s : Rare form of aseptic arthritis/reactive polyarthritis observed in pt of active TB.*

→ *The m/c site for bursitis to occur is the shoulder (subacromial/subdeltoid).*

→ *M/c bursitis in acute knee synovitis is prepatellar bursitis.*

- *Earliest radiological sign is --- haziness of margins of vertebrae (Visible on x-ray only if lesion size is > 1.5 mm and there is 30% or more loss of calcium)*
- **Back pain** is the commonest presenting complaint.
- Cold abscess is m/c complication of early onset paraplegia. These abscesses are paravertebral. Paraplegia may result from compression of cord by cold abscess.
- 3 types of kyphosis (**Gibbus**) is seen
Knuckle kyphosis when 2 vertebrae involved
Angular kyphosis when 3 vertebrae involved
Round kyphosis when >3 vertebrae involved
- **MRI** is investigation of choice to evaluate the type and extent of compression of cord.
- **Clonus** (ankle or patellar) and extensor plantar response is most prominent early sign of Pott's paraplegia.
- Paraplegia in flexion is **grade IV Pott's paraplegia**, in which bowel and bladder are involved. Prognosis is worst in this condition.
- Anterolateral decompression (ALD) - m/c performed operation. Structures removed are rib, transverse process, pedicle and part of body of vertebrae (but lamina is not removed.)

→ *Cystic tuberculosis of bone is best treated by --- Curettage + ATT*

→ *Coke sequestra and sand like sequestra are seen in tuberculosis of bone*

→ *Mortar and pestle appearance, wandering acetabulum seen in TB hip.*

→ *M/c sequelae of tubercular spondylitis in an adolescent is --- bony ankylosis but in peripheral joints /extremities tuberculosis produces fibrous ankylosis*

→ *Pyogenic spondylitis may cause bony ankylosis.*

TB OF BONE/JOINTS**POTT'S DISEASE (Pott's spine/ tubercular spondylitis)**

- Spine is the commonest site of bone and joint T.B (50%).
- M/c site is dorsolumbar junction. (T12-L1); in children upper thoracic spine
- Commonly affects body, lamina, and pedicles but does not affect spinous process?
- **Paradiscal** type of involvement is commonest leading to ↓ of disc space (most consistent radiological sign).

Cystic Tuberculosis of Bone

Most lesions are found in the metaphyses of long bones. They are hyperlucent/ radiolucent, round or oval, and resemble pyogenic infections, aneurysmal and simple bone cysts, cartilaginous tumours or osteoid osteoma.

H/o pulmonary tuberculosis c/b found in some cases.

Curettage f/b ATT for 1 year is the t/t

Spina ventosa

TB of phalanges of hand (TB dactylitis), characterized by lytic lesion on x-ray with new bone formation.

Caries sicca

TB of shoulder joint at time may not produce any pus hence it is called 'Carries sicca'. It should always been considered in d/d of frozen shoulder

Tuberculosis of Hip

Stages

- ① **Stage-I (Stage of synovitis)**— FAbER + Apparent lengthening
- ② **Stage-II (Stage of early arthritis)** — FAdIR + Apparent + True shortening (< 1cm)
- ③ **Stage III (Stage of advanced arthritis)** --- FAdIR + Apparent + True shortening >1cm)
- ④ **Stage IV(Stage of advanced arthritis + subluxation/ dislocation)** --- FAdIR + True shortening Wandering acetabulum may be seen.

X-ray

- ① Haziness of the bones around hip is the earliest sign
- ② Reduced joint space
- ③ **Wandering acetabulum** (The head may be lying out of the acetabulum in the ilium) sometimes appearance of 'pestle & mortar'.

Prolapsed IVD (Intervertebral disc)

- ① **M/c site L4 - L5 & C5-C6** (Posterolateral protrusion)
- ② **M/c nerve root affected L5 & C5 respectively**
- ③ D/g is mainly clinical(MRI should be done before Sx)
- ④ **M/c symptom** : Low backache (± sciatica)
- ⑤ **O/E:SLRT** done for nerve root compression, Lasègue test tendon weakness (d/to L5 compression), absent ankle jerk d/to L₅-S₁ compression
- ⑥ In Myelography:**Root cut-off sign**, block to flow of dye
- ⑦ Medical T/t : Chymopapain (Chemonucleolysis)
- ⑧ Surgical T/t : Percutaneous discectomy, microdiscectomy/ open discectomy.

→ M/c site of dislocation of spine --- cervical spine (Anterior displacement of C5 over C6).

→ Nucleus pulposus hernia is m/c in lumbar vertebrae becoz of weak annulus fibrosis.

& INJURIES

Dislocation of the shoulder

- ① Shoulder is the commonest joint of the body to dislocate & to undergo recurrent dislocation.
- ② Clinically all anterior dislocations are anteroinferior. Common mechanism is a fall on outstretched hand with the **abduction and external rotation of shoulder**
- ③ Bankart's (stripping of glenoid labrum) and Hill -Sach's lesion are seen .
- ④ In anterior dislocation Hill-Sach's lesion is seen in postero-superior head of humerus. But in posterior dislocations the defect lies anteromedially (Reverse Hill Sach lesion).
- ⑤ **O/E** - Patient enters keeping his arm abducted with flat shoulder (+ve Dugga's, Hamilton ruler and Callaway's test)
- ⑥ Kocher's maneuver is m/c used method for reduction.
- ⑦ **C/c** —Recurrent dislocation, injury to axillary nerve

Typical deformities in dislocations

Joint	M/c dislocation	Deformities	C/c or injury to
1. Shoulder	Anterior	Abduction	Axillary n.&a.
2. Elbow	Posterior	IR- rays	Ulnar n., brachial a.
3. Hip	Posterior	F Ad IR	Sciatic n.
4. Knee	Posterior	F,ER	Popliteal artery
5. Ankle	Antero-lateral	Varus	Tibial artery
6. Wrist	Lunate		
7. MP joint	Dorsal (index finger)		
8. Spine	Cervical	Ant. displacement C5 over C6	
9. Foot	Chopart (Inter-tarsal) Lisfrance's (Tarso-metatarsal)		

[Remember 3 'A' of anterior dislocation of shoulder--- Anterior, abduction deformity and axillary nerve injury]

Site of # and nerve injured

Site	M/c nerve involved	Effect
# Humerus		
1. # Surgical neck	Axillary n.	Deltoid paralysis with loss of shoulder contour
2. # Mid-shaft/distal 1/3rd	Radial n.	Wrist drop
3. Supracondylar #	Median n.	Pointing index
4. Medial epicondylar #	Ulnar n.	Claw hand
Dislocation of shoulder	Axillary/ Circumflex humeral n.	Deltoid paralysis
Dislocation of hip (posterior)	Sciatic	Foot drop
# Neck of fibula	Common peroneal n.	Foot drop

Tests for instability of gleno-humeral(shoulder) joint

- Anterior shoulder instability
 - Crank/ apprehension test, Fulcrum test
 - Surprise test (most accurate),
 - Andrew's,
 - Jobe's relocation test
- Inferior shoulder instability
 - Sulcus test
- Posterior shoulder instability
 - Jerk (provocation) test
 - Circumduction, pushpull test

Frozen Shoulder

- Also k/as *periarthritis shoulder or adhesive capsulitis*
- D/s of unknown etiology in middle aged elderly people. A/w diabetes
- Shoulder joint becomes extremely **painful and stiff** d/ to chronically inflamed and contracted fibrotic capsule densely adherent to the humeral head, acromion and biceps
- Diffuse tenderness with disproportionately severe restriction of active and passive motion
- Best T/t is prevention of stiffness by physiotherapy. Treated usually by manipulation under anaesthesia. D/s is self limited; resolves in 1½ - 2 yrs

Impingement Syndrome (Swimmer's shoulder)

- D/s of rotator cuff in which significant impingement occurs when arm is abducted.
- **Supraspinatus** m/s is m/c involved as it passes beneath the acromion and the acromioclavicular joint (*Supraspinatus syndrome*).
- *Rotator cuff tendinitis* is suggested by pain on active abduction (but not passive abduction), pain over the lateral deltoid, night pain, and evidence of impingement sign. Drop arm test is also useful. D/g is made by MRI.

Humerus

Imp. types are

- Upper 1/3rd
- Surgical neck # --- Leads to flat shoulder, seen in elderly women, a/w axillary n. injury
- Shaft of humerus
- Lower 1/3rd of humerus --- Common in children
 - Supracondylar #
 - # Lateral and medial condyle

Supracondylar # of Humerus

- Elbow injury in children may result in a transverse # of the distal end of humerus, above the level of epicondyles.
- Mechanism of injury : fall on outstretched hand with elbow in full extension / pre-extension.
- M/c type : Extension (80%) > flexion. Displacement is backward, upward, & lateral . Distal fragment and soft tissues are pulled by triceps
- O/E there is unusual posterior prominence over point of elbow (tip of olecranon)
 - Three point bony symmetry** is maintained with respect to each other but not in relation to shaft of humerus.
- C/c: Hyperextension injury. M/c complication is malunion resulting in cubitus varus (gun stock deformity). Other c/c are myositis ossificans, VIC, etc.
- M/c artery injured is brachial a. by sharp proximal edge. [Flexors and anterior compartment m/s are affected --- resulting in **VIC** (Volkman's ischemia)]
- M/c nerve injured is AIN (**anterior interosseus nerve**), a br. of median nerve > radial > ulnar (previously radial nerve was considered but now literature suggest AIN). M/c nerve involved in flexion type of # is ulnar nerve.
- T/t
 - CR and immobilization using posterior above elbow plaster slab
 - In late cases : Smith / Dunlop traction c/b applied
 - Absolute indication for operative intervention --- (i) open

#, (ii) vascular/ neural compromise.

- French osteotomy for correction of cubitus varus deformity.

Lateral condyle of humerus

- Involves capitulum and lateral epicondyle
- Salter and Harris type IV epiphyseal injury
- Occurs d/to pull of the common extensor origin
- C/c :
 1. Non- union (commonest c/c)
 2. Cubitus valgus deformity (Gun stock deformity)
 3. Tardy ulnar nerve palsy (late c/c)
 4. Osteoarthritis

Medial epicondyle of humerus

- Commonly a/w posterior dislocation of elbow
- Ulnar n. injury may occur.

→ Lift-off test (Gerber's test) and abdominal compression test are performed to test subscapularis m/s. Internal rotation of shoulder joint is tested.

Conditions a/w limitation (restriction) of Abduction and internal rotation.

- Avascular necrosis
- Perthe's disease (esp. in flexion)
- Slipped capital femoral epiphysis (tendency to ↑ external rotation as hip is flexed)

Supratrochanteric shortening (Shortening of leg) is seen in -

- Dislocation of Hip (anterior / posterior)
- Central # dislocation of Hip (shortening but no rotation deformity).
- Destruction of femur head / acetabulum
- # NOF (intra-capsular)
- Coxa vara
- Mal-united intertrochanteric #

→ Shortening is maximum in --- Posterior dislocation hip & # shaft of femur

→ Shortening of limb is seen in --- Posterior dislocation hip & # shaft of femur, Tom Smith's arthritis

→ Apparent lengthening is seen in --- Obturator type of ant. dislocation of hip

HIP JOINT

Position / attitude of hip..... is seen in

Flexion, Abduction, External rotation (FABER)	Flexion, Adduction, Internal rotation (FADIR)
1. 1st stage TB hip	1. 2nd, 3rd stage TB hip
2. Anterior dislocation hip	2. Posterior dislocation hip
3. # Shaft of femur	3. Traumatic dislocation
4. Polio hip	hip
5. Hip joint effusion	

→ In #NOF attitude of limb is of flexion, adduction & external rotation (FADER). Limb shortening is seen.

→ In extracapsular (intertrochanteric) # of femur exaggerated FADER is seen.

→ In TB of knee joint, RA, Polio

Early stage --- Flexion deformity

Late stage --- Triple deformity (flexion + backward subluxation + external rotation of tibia)

→ In avulsion # of greater tubercle of humerus, movements affected are --- AbER

Clinical tests

Bryants triangle, Nelaton's line, Cheines line, Moore's bitrochanteric line, shoemaker's line.

Lines on the AP X-ray of Hip:

- Nelaton's line --- Line joining ischial tuberosity to ASIS (Passes through tip of greater trochanter)
- Shoemaker's line --- Line joining tip of greater trochanter to ASIS
- Shenton's line --- Line b/w medial cortex of NOF to lower border of superior pubic rami (Breached in #NOF, # head of femur, # sup. pubic rami, hip dislocation)

- Girdlestone's operation or femoral head ostectomy (FHO) is a surgical procedure that removes the head and neck from the femur (femoral head & neck osteotomy). Also k/as excision arthroplasty of the femoral head and neck.

FHO surgery is performed to alleviate pain. It is a salvage procedure, reserved for condition where pain can not be alleviated in any other way. Indicated in hip dysplasia, Legg-Calve-Perthes' d/s, severe septic arthritis (infected) of hip.

- **Coxa vara** : Localised bony dysplasia of the femoral neck. Characterised by a decreased neck shaft angle and the presence of a triangular ossification defect (*Fairbanks Triangle*) of the inferior femoral neck. Results in decreased length of the involved limb. The normal neck shaft angle in a child is $\sim 160^\circ$, which decreases to about 120° in the adult

DISLOCATION OF HIP

3 types

Posterior dislocation of Hip

- M/c type
- Seen in young adults following high velocity trauma (RTA, dashboard injury, *motorbike* accident, bumper injury etc.). Trauma is so severe that the patient will be brought in casualty on strature with severe pain
- LL may appear internally (medially) rotated, adducted and flexed. [Mn--FAdIR]
- There is **shortening** of limb (maximum) & risk of sciatic nerve damage

Anterior dislocation of hip

- Is rare. Seen after severe trauma esp. **fall from tree** or road accident.
- LL may appear externally (laterally) rotated, abducted & flexed in obturator type (or *extended in iliac/pubic type*)
- There is apparent lengthning & risk of femoral nerve damage

Central # dislocation of hip

- Shortening but **no rotation deformity**. Both lower limbs remain parallel to each other
- Femur head can be felt on PR examination.

Congenital dislocation of hip

- Posterior most is most prevalent.
- D/to shallow acetabulum

AVASCULAR NECROSIS(AVN) of Femoral Head

- Aseptic ischemic necrosis (epiphysis is m/c site)
- M/c cause --- idiopathic > prolonged steroid use > post traumatic > sickle cell d/s
- ↓ed range of movt. IR restricted first then abduction

- **MRI** is investigation of choice. *Sectoral sign* is seen in MRI.
- Pathognomonic sign--- **Crescent sign** visible on plain X-ray

Trendelenberg gait Vs Antalgic gait

Trendelenburg's sign /gait (Gluteus medius lurch)	Antalgic gait (<i>Painful</i>)
<ul style="list-style-type: none"> • Caused by weakness of the abductor m/s of the lower limb, gluteus medius & gluteus minimus. 	<ul style="list-style-type: none"> • 3 components ↓ed stance phase + lurch towards same side and grimace on face
<ul style="list-style-type: none"> • Causes are <ul style="list-style-type: none"> - Hip dislocation / subluxation - # NOF, Coxa vara - Neuromuscular d/s, CP, - Tarsal Coalition, Toddler's #, - Lesion of superior gluteal nerve - A/w foot drop (in L5 radiculopathy & after poliomyelitis) 	<ul style="list-style-type: none"> • Causes <ul style="list-style-type: none"> - Infections septic arthritis, osteomyelitis - Rheumatic synovitis - Leg Calve Perthes d/s (coxa plana) (Any cause leading to secondary arthritis)

→ Trendelenburg's sign is positive in weakness/ paralysis of gluteus medius and minimus (injury to superior gluteal nerve).

SCAPHOID

- Common in young adults
- # occurs through the waist of the scaphoid after fall on outstretched hand
- Tenderness is found in scaphoid fossa (anatomical snuff box)
- T/t : Cast is applied in glass holding position (little dorsiflexion and radial deviation)
- C/c : Avascular necrosis, delayed union or non- union, osteoarthritis of wrist
- Proximal segment # is at more risk of avascular necrosis than distal as blood supply enters the scaphoid from distal to proximal.
- Complications are caused by hip spica/ obstruction of hip spica.

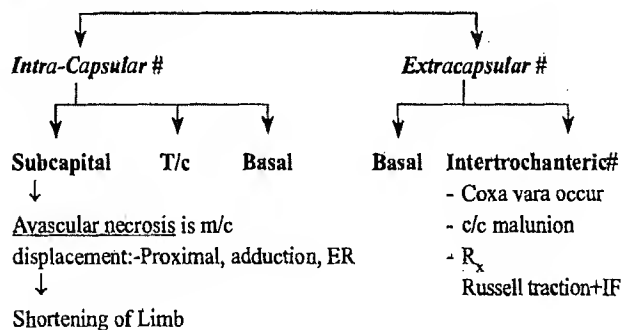
NECK OF FEMUR (# NOF)

- o M/c # in elderly.
- o C/c # acute pulmonary embolism.
- o Deformity of leg
Flexion + adduction + external rotation of leg (FADER);
Shortening of leg /rotation of head of femur

Delbet classification of # NOF in children

- o Type I --- Transphyseal, t/t is CR and +/- fixation
- o Type II --- Transcervical, t/t is CR fix always after CR
- o Type III --- Cervico, t/t is CR and +/-
- o Type IV --- t/t is CR and +/-
- o Type V --- t/t is conservative

Classification



Classification of # NOF in adults/ elderly

- o Given by Powell's, Anatomical, AO, Garden
- o T/t plan in adults
 1. Fresh # --- CR/ OR + fixation with cannulated cancellous screw
 2. Old # --- # NOF 3 weeks after injury
If patient is < 40 year look for viability of femur head.
If head is viable---then achieve reunion by osteosynthesis.
T/t option is fixation with cannulated cancellous screw ± vascularized fibular graft. (Consider Modified Powell's valgus osteotomy for severe transverse #)
If head is non-viable---then modular bipolar prosthesis (THR may be required after 10-15 years in these pt).

Old #			
Head viable		Non-viable	
> 60	< 60	No degenerative change	Degenerative changes in acetabulum
Bipolar	1. Valgus osteotomy 2. Fibular graft with cancellous bone	Bipolar	THR

If patient is 40 year + or an elderly who is physiologically

young or wants to rejoin work then modular bipolar prosthesis

THR is considered if degenerative changes have appeared in acetabulum (e.g. in elderly with osteoarthritis, very old # in a 40+ patient)

- o T/t plan for extracapsular or intertrochanteric #
Proximal femoral nailing (PFN) is better option than DHS.
PFN is a percutaneous procedure with less complications
- Teloscopy test is useful to diagnose intracapsular # NOF.
- Gallow's traction is applied to # shaft of femur in infants and children.
- Fracture NOF & inter-trochanteric femur # both present with lateral rotation and shortening, but deformity is more pronounced in intertrochanteric # (foot touches the couch)
- Avascular necrosis is common in intracapsular / subcapital # NOF while malunion is more common in extra capsular NOF.
- Avascular necrosis and non union risk is maximum in sub-capital # > transcervical > basal > intertrochanteric (but in children maximum risk in transphyseal)

KNEE JOINT, LIGAMENTS AND INJURIES

Medial meniscus	Lateral meniscus
<ul style="list-style-type: none"> o Semicircular [in periphery it is attached to tibial or medial collateral lig.] o Torn more often because it is less mobile o (Being fixed to <u>medial</u> collateral ligament) o Tear most often in <u>its post horn</u> (Bucket handle tears are M/c type) o Injured when a player standing in a semiflexed knee twists his body to one side 	<ul style="list-style-type: none"> o Nearly circular, occupy more tibial condylar surface o Popliteal tendon attaches to lateral meniscus which separates it from fibular / lat. collateral ligament.

- o Surface of menisci has no synovial covering.
- o Cruciate ligaments are intracapsular, extra synovial membranes.
- o Synovial membrane is invaginated posteriorly by the cruciate ligament.

- **Locking** is d/to continuous action of **quadriceps femoris**. Internal or medial rotation of femur on fixed tibia provides stability to the knee joint on standing k/as "Physiological locking"

[Funda: Remember with the action of Lock and key , Consider rt tibia as lock & Rt femur as key. In locking what we do is medial or inward rotation of key & v/v.]

- **Pseudo-locking** is seen in case of loose bodies, hamstring spasm.
- **Un-locking** of knee is d/to action of popliteus muscle (causes lateral rotation of femur on tibia)

→ **Coronary ligament** — is **meniscotibial** component of **medial collateral ligament**

→ **Tests for meniscal injury** - **Mc Murray's & Apley's grinding tests**

→ **Tests for collateral ligaments** — **Apley's distraction test**

→ **Tests for cruciate ligaments (ACL, PCL)** — **Lachman test** is more reliable than ant/ post. Drawer test

→ **Clinical test which is safer to be performed with ease in case of an acutely injured knee joint**—**Lachman test** (because 90° flexion is not possible in acute cases)

→ **MRI is imaging (or non-invasive) modality of choice in meniscal tear.** Arthroscopy is diagnostic

→ **It is wise to repair than remove the torn meniscus provided the tear involves**—**Outer third of meniscus (red-red zone); meniscocapsular junction.** These are vascular zones

→ **Often the injury to medial collateral ligament, medial menisci & anterior cruciate ligament occurs together k/ as Unhappy triad of O'Donoghue.** Functional outcome is poor

Cruciate ligaments

Cruciate ligaments of knee are important in maintaining antero posterior stability of knee joint

Ant. cruciate ligament (ACL)

- Prevents backward displacement of femur on tibial plateau

(i.e. It prevents anterior translation of tibia on femur)

- ACL has much more role in limiting extension of lateral condyle of femur & then causing medial rotation of femur in the screw home position of full extension
- Injured by hyperextension injury (most common ligament injury at knee)

- **Tests** - Ant. Drawer test
- Lachman test (most sensitive)
- Pivot-Shift test
- Celery stalk sign is seen in degenerated ACL.

Post. cruciate ligament (PCL)

- Prevents the femur from sliding forward off the tibial plateau.

(Prevents posterior translation of tibia on femur)

- In the weight bearing knee (flexed knee), it is the only stabilizing factor for femur & its attachment to quadriceps helps in walking downhill/ down stairs

- **Injured during backward force on tibia in semi-flexed knee**

- **Test** → **Post drawer test**

- PCL arises from post part of intercondylar area of tibia (& runs upward, forward & medially) to attach on lateral surface of anterior part of medial condyle.

Collateral ligaments

- **Tibial / medial collateral ligament** --- is degenerated tendon of adductor magnus (injured in valgus injury)

- **Fibular/ lateral collateral ligament** --- is degenerated tendon of peroneus longus (injury is less common).

Varus stress test is positive

- **Stress test:** performed at 30° knee flexion +ve with collateral ligament injury. Valgus stress on the knee is performed to assess tibial collateral ligament.

Apley's distraction test:

→ In meniscal injury recurrent episode of pain & locking must be prevented by terminally extending the knee for last some degree. Knee remains swollen & in position of 10° flexion.

→ **Cylinder cast/ Robert Jones bandage** is used to immobilize knee in cruciate / collateral ligament injury

Tests for anterior instability of knee joint

- **Lachman's test** (more reliable test, indicates ACL injury)
- **Anterior drawer test** (Other peripheral structures e.g. medial meniscus, meniscotibial ligament must also be damaged to elicit this sign)
- **Pivot shift test** (shows damage to the posterolateral corner of the knee joint and the ACL).

Tests for posterior instability of knee joint

- **Posterior drawer test** (positive if there is torn PCL)

Feature	Osteomalacia	Osteoporosis	Osteopetrosis	Osteogenesis Imperfecta
Also k/as	Soft bone d/s		Marble bone./ Brittle bone ds/ Albert's Schonberg ds.	Brittle bone d/s
A/w	Vit D metabolism , hypoparathyroidism, CRF	Post menopausal women d/to ↓ estrogen level, Smoking	AD (AR form is rare but fatal)	AR form is fatal
Mech.	Amount of Ca^{++} accretion per unit bone matrix is deficient in adults	Bone resorption > bone forma ⁿ <i>Matrix & minerals both are lost over time</i>	Loss of ruffled border of osteoclast → ↓ bone resorption , bone overgrowth.	Mutations in <u>type I collagen</u>
Patho- genesis	Osteoid formation is normal but defect in mineralisation of bone matrix (Qualitative)	Bone quality normal (matrix : mineral ratio normal) but ↓ in quantity (amount)	Pathological # are frequent as the bones weak & brittle.	Defective collagen synthesis
Histo	↑ in thickness of osteoid seams	Thin trabeculae that have normal calcification & normal osteoblast & osteoclasts		Woven bone
Cl/F		M/c affect : Long cancellous bone	Obliteration of medullary cavity → anemia , pancytopenia, hepatosplenomegaly	Thin translucent blue sclera, laxity of joint ligaments, deafness d/to otosclerosis, abnormal teeth
X-ray	Washed out bone on X-ray (loss of trabeculae) ↓ Looser's zone (visible at NOF inner side) Milkman # / Pseudo# <u>Tri-radiate pelvis</u> <u>Protrusio acetabuli</u>	M/c site : compression # of vertebrae at D ₁₂ -L ₁ level (usu- ally anterior). D-L spine is the m/c site of weakness. <i>Codfish vertebrae</i>	Chalky white bone deposits, ↑ ra- dioopacity of bones <i>Sandwich vertebrae</i> "Bone within bone" appearance Rugger jersey spine in type 2, Meta & diaphysis wide in long bones → "Erlenmeyer flask" deformity	Multiple # in infant are characteristic, but healing of # is normal
Lab/f	25 (OH) Vit D is ↓ ed , which is most sensitive & earliest marker for nutri- tional osteomalacia, ↑↑ALP	<u>NORMAL serum level of Ca.</u> <u>P, ALP & PTH</u>	Level of Ca, ALP ⇒ N (in adults) may be ↓Ca, ↓PO ₄ ⇒ (in children) ↑ Acid phosphatase	

	Hyperparathyroidism	Paget's d/s (Osteitis deformans)
Patho	↑ bone resorption (osteolytic effect), Irregular & diffuse rarefaction of bone d/to generalised osteopenia	Uncoupling of osteoblastic & osteoclastic activity, Irregular osteoid seams (<i>mosaic/ jigsaw pattern</i>), Stages Clstic/lytic → mixed → last sclerotic stage
Cl/f	Subperiosteal resorption of terminal tuft of phalanges, clavicle & pubic symphysis - Skull--- salt & pepper appearance - Loss of lamina dura, - Thinning of cortex - Expansile lytic lesions k/as brown tumours (osteitis fibrosa cystica)	<i>Cotton-wool skull</i> , Changing hat/ helmet size Osteoclasts are large with ↑ no. of hyperchromatic nuclei & viral inclusions M/c site of 2 ^o osteosarcoma in a pt of Paget's d/s is ---pelvis
Lab/F	↑ ALP often, ↑ Ca	↑↑↑ ALP

DISEASE OF BONE

- Brittle bones are seen in : Osteogenesis imperfecta & Osteopetrosis.
- Osteitis fibrosa cystica is seen in severe secondary hyperparathyroidism (also known as Von Recklinghausen's disease of bone)
- Osteopenia (↓ density of bone) is seen in : Osteoporosis, Osteomalacia & Osteitis fibrosa (Hyperparathyroidism), Multiple myeloma / diffuse metastases.
- Rugger jersey sign is because of osteosclerosis & is seen in : Secondary hyperparathyroidism (CRF), Osteopetrosis & renal osteodystrophy.

Alkaline phosphatase in bone diseases

↑ed in	<ul style="list-style-type: none"> ○ Rickets and osteomalacia ○ Paget's disease ○ Osteosarcoma ○ Carcinoma, osteoblastic metastases ○ Prim. Hyperparathyroidism ○ Fibrosarcoma
Normal in	<ul style="list-style-type: none"> ○ Osteoporosis ○ Osteopetrosis ○ Healing fracture ○ Osteosclerosis ○ Fibrous dysplasia ○ Hypoparathyroidism ○ Multiple myeloma
↓ed in	<ul style="list-style-type: none"> ○ Achondroplasia ○ Hypophosphatasia ○ Cretinism ○ Scurvy ○ Deposition of radioactive substances in bone

BIOCHEMICAL MARKERS OF BONE METABOLISM

	Serum Ca ⁺⁺	Serum PO ₄ ⁻	Serum ALP	Serum PTH	25 (OH) vit D	1,25DHCC or Vit D3	Remark
Normal	(9-11 mg%)	(3-4.5 mg%)	(30-120 U/L)				
Osteoporosis	N	N	N				↑ ALP after a healing #
Paget's ds	N	N	↑↑				Hypercalcemia may occur after immobilization
Nutritional Osteomalacia	N	↓	↑/N	↑	↓	Variable	25 (OH) Vit D is earliest & most sensitive marker for nutritional osteomalacia
Rickets							
- Nutritional	↓	↓	↑	↑ (2°)		↓	
- VDDR (Hypophosphatemic)	N	↓↓	↑	N			X linked -D, Defect in renal tubular PO ₄ ⁻ reabsorption
- VDDR - I	↓	↓	↑	↑ (2°)			AR Def. of 1-α hydroxylase
- VDDR - II	↓	N	↑				End organ resistance to 1,25 DHCC d/to its nuclear receptor mutation
Hyperparathyroidism	↑	↓	↑				
Hypoparathyroidism	↓	↑	N				Same in pseudo hypo PTH
Renal osteodystrophy	↑	↑↑	↑				
Hypophosphatasia	N, ↑	N	↓↓				↓ hydroxyproline in urine
Osteolytic bony metastases	↑	-	↑				↑ hydroxyproline in urine
In osteoblastic secondaries	↓	-	↑				-
Multiple Myeloma	↑	variable	Normal				

BONE GRAFTING

- Chip grafts are obtained from --- Cancellous bone
- M/c site for taking (harvesting) bone graft --- Iliac crest
- Graft primarily provide a scaffolding, upon which new bone is laid down. (Osteoconduction)
- Muscle pedicle bone grafting --- Non union # NOF (Bakshi Operation or Meyer's operation)
- Cancellous bone graft --- for healing (iliac crest) ⇒ sliver / strip graft
- Cortical bone graft --- is for support (fibula, tibia) ⇒ Slab graft
- M/c type of graft used in India --- autograft
- Allograft bone is preserved by --- by deep freezing (-70°C), by decalcifying it, and by formalin preservation
- Artificial graft --- Hydroxyapatite with porous structure. Used in orthodesis at periphery of woven bone.
- **Shephard -Crook deformity** refers to coxa varus angulation of the proximal femur (fibrous dysplasia).

Loose bodies are seen in

- Osteoarthritis
- Osteochondritis dissecans
- Osteochondral #

Bony ankylosis (fusion) may result from

- Pyogenic arthritis (m/c cause)
- Tubercular arthritis of spine
 - *Tuberculous arthritis of hip, knee and spine (tubercular spondylitis) result in --- fibrous ankylosis*
 - *Tuberculous arthritis of small/ peripheral joints result in --- fibrous ankylosis*
 - *Pyogenic arthritis of peripheral joints as well as spine (spondylitis) results in --- bony ankylosis.*
 - *Syphilitic arthritis m/c involve knee joint.*

Septic (Pyogenic) Arthritis

- M/c site knee
- M/c organism implicated in s~ is *S. aureus*. In adolescents/ young adults *N. gonorrhoeae* is m/c
- Chondrolysis is common in infancy
- S~ is the m/c cause of bony ankylosis.

Osteomyelitis

- M/c organism in all age group --- *Staph. aureus*
- Almost invariably a disease of children
- M/c site is **metaphysis** of long bones in children (**lower end femur** > upper end tibia). In adults thoracolumbar spine is

the m/c site

- M/c mode of infecⁿ --- hematogenous. Stasis of blood d/to "hair- pin tuft arrangement" of vessels in metaphysis which promotes growth of organism
- **Sequestrum** is the hallmark of the chronic osteomyelitis. Sequestrum is a dead piece of bone, lighter than live bone and acts as a nidus for infection. Sequestrum is the m/c cause of non-healing sinus in chronic OM.

Various types of sequestra:

Type of Sequestra	Found in
1. Ring	Amputation stumps, Around pin tracks (external fixators)
2. Tubular	Hematogenous OM, mid segmental #
3. Rice grain/ feathery	Tubercular

- **Involucrum** is periosteal new bone around necrotic sequestrum
- C/c are fractures, sepsis, chronic OM. **SqCC** is the m/c malignancy seen in chronic osteomyelitis
- TOC - i.v. Antibiotics

Specific Osteomyelitis

1. HIV osteomyelitis

Usually B/L, necrosis absent, periosteal new bone formation.

2. Tubercular osteomyelitis

- Osteoarticular tuberculosis is generally paucibacillary hematogenous d/s. (Secondary tuberculosis).
- Inflammatory features & periosteal reaction are uncommon
- Sequestrum is uncommon (Rarely 'Feathery' or "rice grain" sequestrum may be seen)

→ *The earliest change noted in X-ray in a case of acute osteomyelitis --- Periosteal reaction*

→ *Osteomyelitis in a patient of sickle cell d/s (SCD) is most specifically caused by --- Salmonella*

→ *Bony changes seen in syphilis are --- osteomyelitis, arthritis, osteochondritis, osteosteitis and periosteitis in late congenital syphilis.*

→ *Knee joint is most commonly involved in syphilitic arthritis.*

→ *In osteoarthritis, quadriceps m/s is m/c affected*

Garré's OM

- Sclerosing, non-suppurative chronic osteomyelitis.
- Fusiform osseous enlargement in shaft of femur/ tibia. No discharging sinus

Brodie's abscess

- Sub-acute osteomyelitis which leads to long standing localized pyogenic abscess in metaphysis of femur / tibia
- Deep boring pain which becomes worst at night

Tom - Smith Arthritis

- Septic arthritis of hip in infant.
- Child presents with limp, unstable gait. Affected leg is short & movements ↑ in all direction (*Limping without pain*), *telescoping of hip*, **supratrochanteric shortening**
- X-ray shows complete absence of head & NOF.

Generalised osteosclerosis is seen in

- Blastic secondaries (e.g. from prostate)
- Osteopetrosis, Renal osteodystrophy,
- Fluorosis
- Caffey's d/s, Paget's d/s, Engelman's d/s

↑ed Radioisotope uptake is seen in

1. Bony metastasis esp. of axial skeleton
2. Degenerative joint d/s, inflammatory joint d/s
3. Traumatic #, Post surgery
4. Paget's d/s, Metabolic bone d/s, Dental d/s (fluorosis)
5. Infection

Poliomyelitis

- *Asymmetric flaccid (motor) paralysis without any sensory loss (non progressive)*
- Affects AHC of lumbar enlargement
- Lower limb commonly affected
- Partial m/s paralysis is more common and it most commonly affects quadriceps femoris.
- M/c m/s undergoing complete paralysis is tibialis anterior.
- M/c muscle affected in hand---opponens pollicis
- Bulbospinal p~ is most life threatening because it affects motor neurons of medulla
- Deformities in late stage-

Hip	Knee	Foot
Flexion	Flexion (m/c)	Equino varus (m/c)
Abduction	Triple deformity	
Ext. rotation	- Flexion	
	- Posterior subluxation	
	- Ext. rotation	

- In upper limb elbow & shoulder affected (Muscles of hand/ wrist are usually spared)
- R_x:

Sautter's / Campbell release	---	for Hip
Wilson's release	---	for knee
Tendon lengthening	---	for Equinus
Stendler's release	---	for cavus
Soutters, Yount procedure	---	for TFL contracture
- Tendon transfer should **not** be done before 5 yrs of age

SCOLIOSIS

- Is sideways curvature of the spine.
- It can be of two types
 - (i) Non structural or transient — (postural, compensatory and sciatic scoliosis)
 - (ii) Structural or permanent — **Idiopathic, congenital, paralytic** and others.
- A/w restrictive lung d/s, Rickets
- M/c complain is visible deformity; pain may be an occasional features.
- **Radiological features :**
 - Cob's angle** an angle b/n the lines passing through the margins of the vertebrae at the ends of the curve. (Measures severity of the curve).
 - Reisser's sign** is because of fusion of iliac epiphysis with iliac bone. It indicates maturity and there is no possibility of curve worsening.
- For Scoliosis **Milwaukee brace**, Boston brace, Reissner's turnbuckle casts are used. **Cotrel traction** is also applied pre-operatively.

PHYSIOTHERAPY & SPORTS MEDICINE**Modalities to relieve musculoskeletal pain**

Heating modality	Example	Based on
Superficial heating modalities	Heat packs	
	Infra red - rays	
	Paraffin bath	
Deep heating modalities	Hydrotherapy	
	Short wave diathermy	27.12 MHz radiofrequency
	Microwave diathermy	EM radiation
	Ultrasonic heating	High frequency (0.8-1 MHz) acoustic vibrations

- Deep heat therapy is use to relieve pain in inflammation of joints / tissue, m/s spasm, etc.
- Short wave diathermy involves the therapeutic application of high radio-frequency of 27.12 MHz.
- The activity to be avoided to prevent worsening of lymphedema is --- Isometric exercises
- The activity to be avoided in cerebral palsy --- massage

Interferential therapy

- Used for : Pain relief, m/s stimulation, ↑ local blood flow, and to ↓ edema.
- Used to relieve pain in traumatic neuroma at the site of amputation.

Athletics Pubalgia

- Also k/as sportsman hernia or Gilmore's groin , affects athletes especially soccer and hockey players
- C/by chronic groin pain and widened SIR. Pain is aggravated on hip extension, radiates down to testicles and adductor region.

Insertional Tendinitis of Tendoachilles

- M/c cause is improper wearing of shoes.
- It is a slow, insidious process of gradual enlargement and pain at the insertion of the Achilles tendon. Progressive difficulty with wearing of closed-back shoes and pain after a period of rest, such as on first arising in the morning, are noted.

Prosthetic feet

- SACH : Solid Ankle Cushion Heel. Provides pseudoplatar flexion. Prescribed in people with b/L amputations.
- SAFE foot: Stationary attachment Flexible Endoskeletal. Good choice for elderly. Permits triplanar movements and an easy rollover.
- Dynamic response feet: Indicated for people with energy storing gait .

PEDIATRIC ORTHOPAEDICS

CTEV (Clubfoot)

- Incidence of clubfoot or CTEV is 1 in 1000 live births. (M/c orthopedic congenital anomaly in India)
- There is inversion of hindfoot, adduction of forefoot, and limited dorsiflexion - an equinovarus deformity.

- Common in males. B/L in 60% cases.
- Congenital equinovarus of foot has been reported to occur in families as autosomal dominant trait with incomplete penetrance.
- *Tibialis posterior* is the most imp. m/s related to pathology of clubfoot.
- Deformity involves medial subluxation of the navicular and calcaneus on the talus. Joints principally involved are thus the subtalar and the talonavicular joints.
- **Equinus** deformity occurs primarily at the ankle joint. **Inversion (varus)** deformity occurs primarily at the subtalar joint.
- *Secondary clubfoot* occurs in paralytic disorders (e.g. polio, spina bifida, myelodysplasia, freidreich's ataxia, arthrogryposis multiplex congenita).
- T/t should begin soon after birth
- T/t in newborn --- Manipulation by mother + adhesive strapping/Dennis -Brown splint/casting (Ponsetti technique is advised now a days)
- (< 1 month)
- 1 month-6 month --- Corrective manipulation + above kneecast
- 6 month - 3 yr --- Soft tissue release (posteromedial)
- 4-8 yr --- Litchblau's procedure (<6 yr) or **Evan's Dweller operation** (>6 yr) resection & fusion of *calcaneocuboid*
- 8-12 yr --- Wedge tarsectomy
- > 12 yr --- Triple orthrodesis
- **Triple arthrodesis** involves fusion of TN, TC & CC (Talo-Navicular, Talo-Calcaneal, Calcaneo-Cuboid)
- Order of correction A → I → E (adduction deformity is corrected first) [Mn : AIE for All India Examination] If not corrected in this order Rocker bottom foot (d/to fixation at midtarsal jt) may result
- **Ponseti technique** is now used for correction of foot by manipulation and casting.
- D/D : In Arthrogroposis multiplex congenita , the clubfoot is more rigid and the dorsum of the foot can not touch anterior tibia.

DDH (Developmental Dysplasia of Hip)

- Earlier it was called CDH.
- IOC is ultrasound.
- Otolani maneuver is done at birth to r/o DDH in newborns.
- IOC is ultrasound.

Congenital Vertical Talus (Rocker Bottom foot)

- Foot everted into valgus
- Convex plantar surface

Flat foot (Pes planus)

- Foot has an abnormally low or absent medial arch (MLA).
Calcaneo-navicular fusion.
- Forefoot is abducted, producing planovalgus foot.
- Tarsal coalition

Legg- Calvé Perthes Disease

- A form of osteochondritis of the hip joint.
- C/F : A painful or antalgic gait is present, ↓ range of hip movements (*especially abduction and internal rotations are limited*) and sometimes flexion- adduction contractures
- D/to ↓ hip motion deformity is of attitude of --- Adduction and ER of hip with shortening of limb
- Idiopathic avascular osteonecrosis of the capital femoral epiphysis of the femoral head.
- Boys 2-12 years commonly affected. 15-20% have B/L disease
- **On x-ray:-** *hip joint space is ↑ed (coxa magna)*
- **T/t:-** Containment of head conservatively or by osteotomy.
Abduction and stretching exercises are useful.

Genu Varum (Bow legs)

- There is varus deformity at knee
- Causes of **genu varum** (Bow legs)
Idiopathic (physiological) > Blount's ds (tibia vara) > Rickets

Genu Valgum (Knock knee)

- There is valgus deformity/knocking at knee.
- Usually a/w flat foot
- Causes are
 1. Idiopathic (physiological): M/c cause. Appears at 2-3 yr of age. Always corrected spontaneously by 6 yrs
 2. Post traumatic
 3. Renal osteodystrophy

Genu Recurvatum

- There is hyperextension at knee joints.
- Causes of **genu recurvatum** (Hyperextension of knee)
Congenital > Polio (m/c acquired cause) > Marfan's

Congenital Torticollis

Twisted neck present at birth is m/c d/to muscular cause. A/w

positional deformity, Klippel-Feil syndrome, hemivertebrae, atlanto-occipital fusion or -nt sternomastoid on one side. Sometimes it is seen in breech extraction. Passive stretching and splinting is the t/t but most cases resolve spontaneously. Untreated cases progress to facial asymmetry and plagiocephaly.

Imp points from pediatric orthopaedics

- Leg length discrepancy is -nt up to 3 yr. but obvious after 4 yr.
- **Birth #** : Usually uncommon, but 75% occur in association with breech delivery. Although 92% of birth injuries are clavicular # (these involve diaphysis rather than epiphysis) M/c site of epiphyseal injury with birth trauma in ↓ing order of frequency :- proximal humerus > distal femur > distal humerus > proximal femur > distal tibia.
- **# in child abuse** : # of multiple ages at various sites present rib # (most common) > humerus
- **M/c joint dislocation** in a child's hand --- MCP Joint
- **In # scaphoid** distal pole is more frequently #ed in children (while waist in adult) displacement is uncommon
- **Green stick #** : One cortex is completely disrupted. Other undergoes plastic deformation, which results in angulation/rotation of the bone or both. Angular deformity is more likely to recur.
- **M/c site of terminal bony overgrowth** in children with acquired amputation is → Humerus > fibula > tibia
- **Stress # in children** → tibia > fibula > tarsal, meta tarsal > talus > proximal femur
- **Stress# in adult**: metatarsals > fibula > tibia > femur neck
- **Many # unites readily despite almost constant movt between fragments** [ex. # ribs, clavicle or shaft of femur (angulatory movt is not harmful). Movements that are harmful and responsible for non-union / mal-union are -- rotatory/shearing movements liable to occur in # of forearm bones, # of scaphoid & in #NOF
- **Remodeling** is greatest when the # is near physis & when the deformity is in the plane of motion of joint, it is minimal when angulation is at right angles to plane of motion of joint (as in varus angulation of supracondylar #). Remodeling in the diaphysis is largely a process of rounding off the angularity of the bone, so significant remodeling exist for femoral shaft # in a 6yr old child#
#Remodeling will be less effective in
 - Displaced intra articular #
 - Diaphyseal #
 - Malrotation

- Deformity not in plane of joint axis of motion
- Rotational deformities

SOME POINTS OF SPECIAL MENTION

- **# In fall from height:** Axial skeleton is involved; calcaneum (MC) > spine
- **# common in osteoporosis :** # NOF, # of vertebral bodies, Colles#
- **Ant. talofibular ligament is the m/c ligament injured at ankle joint** (in inversion with plantar flexion)
Calcaneofibular Ligament - injured during inversion & dorsiflexion.
- All the sites of active bone resorption around prosthetic component are predominantly populated by macrophage
- MRI is the most sensitive & specific procedure for early detection of avascular necrosis of humerus/femur.
- Ulnar nerve repair has worst prognosis in nerve repair because of the fact that it is primarily a motor nerve.
- Radial nerve repair has good prognosis in nerve repair.
- **Phalen's test** is +ve in carpal tunnel syndrome. Exacerbation of symptoms on forced flexion of wrist.
- **Modified Allen's test** is used for patency of radial artery
- **Thomas test** is used for identifying fixed flexion deformity of hip. Also useful to measure deformity in lumbar lordosis
- **Caffey's disease** is osteomyelitis of jaw. Seen in infants below 6 months. T/t Penicillin.
- Mandible is **the m/c** site for actinomycosis.
- Critical vascular zone of spine is T4 - T9
- Artery of Adam Kweicz extends between T9 - T11
- **Myodesis** is suturing of fasciae and muscles directly to the distal residual bone through drill holes in order to achieve better prosthetic control and function. Myodesis is *contraindicated in presence of ischemia* (severe peripheral vascular diseases)
- **Order of repair during reconstruction of an amputated limb is:**
 1. Internal fixation of bone is done first
 2. Repair of extensor the flexor tendons
 3. Repair of arteries, nerves and veins in that order
 4. Closure or covering of wound
- Rate of mineralisation of a newly formed bone c/b best estimated by --- Labeled tetracycline
- M/c cause of death after THR --- Pulmonary embolism
- Supra-trochanteric shortening can be accurately measured by --- Bryant's triangle
- Position of greater trochanter can be assessed by --- Nelaton's line, Shoemaker's line
- Morris bistrochanteric test is used for --- Detecting inward inclination of the greater trochanter
- Telescopy is used to test --- Stability of a hip
- **Velpeau dressing or a sling-and-swath bandage** is used in acromioclavicular pin fixation (Phemister, modified)
- Watson-Jones operation is a lateral approach to hip (proximal shaft and trochanteric region of femur)
- **Risser's cast** is useful in congenital/ idiopathic scoliosis.
- Metal on metal articulation is avoided in females of child bearing age and inflammatory arthritis.
- When an athlete sits on table with 90° flexion of his knee, tibial tuberosity moves towards lateral border of the patella.
- In SCFE, AP view hip reveals **Trethowan's sign** (Growth plate is displaced towards the metaphyseal side. A line drawn along the superior surface of the neck remains superior to the head unlike in a normal hip where it passes bisecting the head)
- In L5 radiculopathy, there is weakness of dorsiflexion, and extension of great toe, with some weakness of knee flexion. Most severely affected m/s are : EHL, EDL, Gluteus medius.
- **Generalised increased bone density (osteosclerosis) is seen in**
 1. Myeloproliferative d/s --- Myelosclerosis phase
 2. Metabolic ---- Renal osteodystrophy (secondary hypoparathyroidism)
 3. Fluorosis
- **Multifocal > Generalised increased bone density**
 1. Neoplastic --- Osteoblastic metastases (Prostate and breast secondaries), lymphoma, Mastocytosis,
 2. Metabolic --- Paget's d/s
- *In hyperparathyroidism there is osteopenia (generalised decrease in bone density). Other conditions a/w generalised osteopenia are--- osteoporosis, osteomalacia, diffuse infiltrative bone diseases like multiple myeloma and leukemia.*
- Synovial fluid is derived from synovial capillaries and modified by secretory activity of type B cells.
- **Common peroneal nerve injury** is seen in trauma about knee, rupture of fibular collateral ligament, # of fibular neck, # of fibular head, casts etc. Consequences are : Foot drop, sensory loss to web space b/w great toe and second toe.
- Column concept of spine was given by Dennis.

SOME IMP. NEGATIVE POINTS

- Bony change NOT commonly seen in syphilis --- Osteomyelitis
- NOT indicated in acute osteomyelitis --- Surgery
- Movement NOT limited in Perthes disease --- Adduction movement
- Alkaline phosphatase is NOT elevated in --- Hypophosphatasia
- **3- Point symmetry of bone is NOT disturbed in** --- **Supracondylar #**
- NOT a complications of chronic osteomyelitis --- Myositis ossificans
- Flexible flat foot is NOT seen in --- Vertical talus
- Pathological # is NOT seen in --- Flurosis, Osteochondroma
- Loose bodies are NOT seen in --- RA
- Joint NOT involved in RA acc/to 1987 modified ARA --- Tarsometatarsal Joints
- Areas NOT commonly involved in pelvic # --- Ischial tuberosities
- NOT common in TB spine --- Maintained IVD space
- Shortening of leg is NOT seen in --- Obturator type of anterior dislocation hip
- Recurrent dislocation is NOT seen at (uncommon in) --- Ankle joint > patella
- # NOT seen in fall from height --- # fibula
- Internal fixation is NOT required in children --- # Shaft of femur
- Avascular necrosis is NOT seen in --- # Olecranon
- NOT involved in blow out # of orbit --- # of orbital Rim
- NOT seen in articular cartilage with increase in age --- Water content decreases
- Progressive scoliosis is NOT a/w --- block vertebrae
- Drug which does NOT decrease bone resorption in osteoporosis --- Teriparatide
- NOT seen in articular cartilage --- Water content

CLINICAL VIGENTTES

- An HIV positive male on antiretroviral therapy presented with pain in the right hip for last six months with reduced abduction and internal rotation. The most probable diagnosis is:

[AIPGMEE 2008]

- A. Septic arthritis of hip
 - B. Avascular necrosis of hip
 - C. Secondary osteoarthritis of hip
 - D. Tuberculosis of hip
- (Ans. B. Avascular necrosis of hip)

Septic arthritis of hip and secondary osteoarthritis of hip are unlikely because

- Septic arthritis of hip has acute onset, a/w high fever, sudden onset pain. Passive movements are painful.
- In Secondary OA of hip there must be some primary pathology in the hip which is not mentioned in the question.

Now coming to remaining options

- In Avascular necrosis of hip --- abduction and internal rotation are restricted. Use of anti-retroviral drugs predispose to the development of AVN of hip
- In tuberculosis of hip --- there will be global restriction of movement.

- A 65 year old diabetic male presents with 1 year history of swelling of the left ankle joint. On examination the joint is warm, erythematous and unstable. X-rays show disorganized joint with sclerosis of bones, multiple osteophytes and bone formation in soft tissues. All the following can be advised in the management **except**:

[AIPGMEE 2008]

- A. Limitation of activity and bracing
 - B. Arthrocentesis and compression bandage
 - C. Arthrodesis of ankle joint
 - D. Total ankle joint replacement
- (Ans. D. Total ankle joint replacement)

As the joint is warm, erythematous and unstable, It indicates acute inflammation and total ankle joint replacement is contraindicated in this condition.

- A 32 year old male met a road traffic accident . He was brought to casualty on strature . On physical examination his right lower limb was short, internally rotated, flexed

and adducted at the hip. Most likely d/g is

[DNB HRH Delhi'08, AIPGMEE'03]

- A. Fracture neck of femur
- B. Posterior dislocation of hip
- C. Central # dislocation of hip
- D. Intertrochanteric #

(Ans.: Posterior dislocation of hip)

- A 62 year old female slipped in bathroom and sustained injury to her right lower limb. There is shortening of his right lower limb. Limb is externally rotated, adducted and flexed. Most likely d/g is

[DNB HRH Delhi'08, AIPGMEE'03]

- A. Fracture neck of femur
- B. Posterior dislocation of hip
- C. Anterior dislocation of hip
- D. Intertrochanteric #

(Ans.: A. Fracture neck of femur)

Patients profile and diagnostic clues

Anterior dislocation of hip: is rare. Seen after severe trauma esp. **fall from tree** or road accident. Attitude of limb is of FAbER (Flexion + Abduction + External rotation)

Posterior dislocation of hip: is more common. Seen in young adults following high velocity trauma (RTA, dashboard injury, *motorbike* accident, bumper etc.). Trauma is so severe that patient will be brought in casualty on strature with severe pain. Deformity is FAdIR

Central # dislocation of hip: Both lower limbs remain parallel to each other. there is **no rotation deformity**. Femur head is palpable on PR examination

Fracture neck of femur: Common in elderly females (age group 60+) . Occurs after trivial trauma e.g. slip in a bathroom. Deformity is FAdER + shortening

Intertrochanteric #: Common in males of age group 70-80 . Mode of injury is significant. Deformity is exxagerated FAdER + shortening. Foot touches the couch because # is extracapsular

- Raju, a 10 year old child, presents with predisposition to fractures, anemia, hepatosplenomegaly and a diffusely increased radiographic density of bones. Most likely d/g is

[AIPGMEE'02]

- A. Osteogenesis imperfecta
- B. Myelofibrosis
- C. Osteoporosis
- D. Osteopetrosis

(Ans.: D. Osteopetrosis)

- A patient sustained injury to his right upper limb 3 years back. Now he presents with valgus deformity in the elbow and parasthesias over the medial border of hand. The injury is likely to have been-

- A. Supracondylar # of humerus
- B. Lateral condylar # humerus
- C. Medial condylar # humerus
- D. Posterior dislocation of humerus

(Ans.: B. Lateral condyle # humerus)

Tardy ulnar nerve palsy is a delayed c/c of # lateral condyle humerus. Fracture is often a/w cubitus valgus deformity

- A 7 year old child presented to emergency department with pain in left hip joint for last 2 days. On physical examination he is keeping the hip flexed and abducted and does not allow passive movements. Hemogram is normal and ESR is modestly elevated. The most appropriate line of action would be: -

[AIIMS May'2009]

- A. Admit and observe
- B. Ambulatory observation
- C. USG guided needle aspiration
- D. I.V. antibiotics

(Ans. C. USG guided needle aspiration)

The boy in question is most likely suffering from transient synovitis of hip. Transient synovitis of hip is a common inflammatory but sterile condition of hip seen in 5-8 yrs children, char/by painful hip. CBC is usually normal and ESR is modestly elevated. Usual t/t is admit and observe.

If movements are restricted it means effusion has been developed and it should be aspirated under USG guidance to reveal whether a septic hip is present (*Nelson*)

- A 12 yr old boy c/o pain in right hip with fever, gait limping, flexion deformity of right hip. Rotations, education and adduction are normal. No true limb length discrepancy is seen. Based on these findings, the most likely diagnosis is:

[MP'07]

- (A) Tuberculosis of right hip
- B. Septic arthritis of right hip
- (C) Iliopsoas abscess

D. Transient synovitis

(Ans: (C) Iliopsoas abscess)

D/d of painful limp in a child

Tuberculosis hip --- Limb length discrepancy present, low grade fever, insidious/ gradual onset, FADER attitude in stage II & III (FabER in stage I)

Septic arthritis hip --- Pain, swelling, fever, limp, severe limitation in joint movt. (FABER attitude of hip joint), pseudoparalysis like picture

Iliopsoas abscess --- Movements are normal, no shortening. Pseudoflexion deformity +nt.

Transient synovitis --- Common in 4-6 yrs children, painful stiffness of hip

- A 6 year old boy presents with pain in left hip. Movements are persistently restricted with tenderness in the triangle. X ray is normal. Best treatment for him is:

[AIPGMEE 2011]

- A. Ultrasound hip
- B. MRI
- C. Traction with IV antibiotics
- D. Wait and watch policy

(Ans: A. Ultrasound hip)

Possibilities are transient synovitis, septic arthritis and Perthe's d/s. X-ray alone is not informative but an ultrasound is essential to rule out fluid in the joint space. If the fluid is minimal then only NSAIDs and rest will suffice. If the effusion is large and thick USG guided aspiration is necessary alongwith antibiotic cover.

- Ramu, a 8 years old child presents with pain in the arm . X-ray upper end humerus revealed an expansile lesion in the metaphysis with breach of the overlying cortex. Most likely d/g is

[AIIMSMay'02]

- A. Aneurysmal cyst
- B. Unicameral cyst
- C. Chondroblastoma
- D. Osteoclastoma

(Ans: A. Aneurysmal bone cyst)

Aneurysmal bone cyst is an expansile metaphyseal lesion, where as unicameral or simple bone cyst is non-expansile. Breach in overlying cortex is seen in both aneurysmal cyst and osteoclastoma (GCT). Osteoclastoma usually presents after skeletal maturity.

- A patient with multiple injuries developed fever, tachycardia, tachypnoea, rashes around umbilicus on 2nd day. What is the most likely cause is [AIIMS Nov'08]

- A. Fat embolism
 - B. Pulmonary embolism
 - C. Meningitis
 - D. Drug hypersensitivity
- (Ans: A. Fat embolism)

- Meningitis is unlikely within 48 hours of trauma
- In drug hypersensitivity there should be history of exposure to drug and rashes should be generalised.
- **Fat embolism** is common after long bone # esp shaft of femur, usually seen 12 to 72 hours after #, Et CO₂ levels fall to zero

Fat embolism syndrome

- Fat embolism of lungs typically appears 12 to 72 hours (lucid interval) after long bone # especially of the femur or tibia.
- Also observed or a/w acute pancreatitis, parenteral nutrition of lipids, liposuction, cardiopulmonary bypass etc.
- Triad of **arterial hypoxemia, mental confusion (delirium) and petichiae** especially over ant. neck, shoulders and chest.
- Gurd's criteria is used for clinical d/g of FES.
- Arterial hypoxemia is always present and may progress to ARDS.
- In cerebral F~ retinal vessels involved. **Cerebral purpura** in white matter of brain may occur.
- Lipiduria (**fat globules in urine**)
- T/t-O₂ and high dose glucocorticoids prophylactic is used.

Venous air embolism

Is common during surgery above the level of heart (of head / neck region) esp in sitting position. Usually seen during surgery. Signs are unexplained hypotension, tachycardia and sudden decrease in Et CO₂ levels.

- A 68 yr old man presented with complaints of pain in the back. O/E - there is marked reduction in the spine movements. Neurological examination is normal. Chest expansion is mildly reduced. ESR-50mm in 1 hr. X-ray of the back shows syndesmophytes. What is the diagnosis?

[AIIMS May'10]

- A. Ankylosing spondylitis
- B. Degenerative osteoarthritis of the spine
- C. Lumbar canal stenosis
- D. Ankylosing hyperostosis

(Ans. A. Ankylosing spondylitis)

- ❑ AS is a chronic arthritis which mostly affects spine and sacro-iliac joints. F/H and HLA-B27 association is seen.

X-ray LS Spine shows squaring of vertebral body and syndesmophytes (calcified ligaments of IVD)

- ❑ ESR is normal in ankylosis hyperostosis.
- ❑ Chest expansion is not affected in degenerative osteoarthritis of the spine.

- ❑ Person with non united # of distal 1/4th of tibia with multiple puckered scar, discharging sinus and 4 cm shortening. Which is the best line of management.

[AIIMS Nov'09]

- A. Illizarov's fixation
- B. Plating
- C. External fixator
- D. Interlocking

(Ans. A. Illizarov's fixation)

Illizarov's fixation is preferred for resistant nonunion with shortening of limb. Non union is likely in this case as there are signs of secondary infection and complications

- ❑ A 10 yr old child comes to you with h/o swelling of the middle of the thigh with a past h/o trauma 2 yrs back. He has mild fever with raised ESR. X -ray shows concentric periosteal reaction in the shaft of femur. Most logical step in diagnosis is:

[AIIMS Nov'09]

- A. Core biopsy femur
- B. MRI
- C. Bone scan
- D. TLC and CRP

(Ans. B. MRI)

- ❑ A 35 yr old lady presents with chronic backache. X -ray shows collapse of D₁₂ but intervertebral disc space is maintained. All are the possible causes except:

[AIIMS Nov'10]

- A. Multiple myeloma
 - B. Osteoporosis
 - C. Metastasis
 - D. Tuberculosis
- (Ans. D. Tuberculosis)

Intervertebral disc space is reduced in TB and it is the earliest sign of paradiscal Pott's spine.

In osteoporosis, osteomalacia IVD space is normal or slightly increased.

The adjacent discs spaces (IVD) are usually normal in trauma, eosinophilic granuloma, and bone secondaries.

- ❑ A 62 year old lady presented with pain and swelling of right knee for last 2 yrs. Weight bearing radiograph of the knee shows grade III osteoarthritic changes in the knee. Next best step is : [AIPGMEE 2011]

- A. Trial of conservative treatment
- B. Arthroscopic washout of knee
- C. Total knee replacement
- D. Partial knee replacement

(Ans. C. Total knee replacement)

Gr III OA of knee requires TKR while Gr I and II can be managed conservatively.

- ❑ A 6 year old boy presents with pain in left hip. Movements are persistently restricted with tenderness in the triangle. X ray is normal. Best treatment for him is:

[AIPGMEE 2011]

- A. Ultrasound hip
- B. MRI
- C. Traction with IV antibiotics
- D. Wait and watch policy

(Ans. A. Ultrasound hip)

Possibilities are transient synovitis, septic arthritis and Perthe's d/s. X-ray alone is not informative but an ultrasound is essential to rule out fluid in the joint space. If the fluid is minimal then only NSAIDs and rest will suffice. If the effusion is large and thick USG guided aspiration is necessary alongwith antibiotic cover.

- ❑ A teenage girl presents with pain in knee while climbing stairs, and also on standing after sitting for a long time. Probable d/g is :

[AIPGMEE 2011]

- A. Chondromalacia patellae
- B. Bipartite patella
- C. Patello-femoral osteoarthritis
- D. Plica syndrome

(Ans. A. Chondromalacia patellae)

Chondromalacia patellae is common condition which usually affects teenage girls. These girl usually present with pain on anterior aspect of knee, which is exaggerated on

climbing stairs or walking after long period. It is usually caused by abnormal loading of femoropatellar joint. Rest and quadriceps exercises are advised.

- A 35 yr old man presents with back pain after lifting heavy weight. He also had pain on lateral side of right leg with loss of sensation of right great toe. What is the probable diagnosis: [AIPGMEE 2012]

A. L2L3 disc prolapse

B. L3L4 disc prolapse

C. L4L5 disc prolapse

D. L5S1 disc prolapse

(Ans. C. L4L5 disc prolapse)

- A 4 yr old girl presents with rapidly gaining weight and height since last 11 months has inability to sit with crossed legs and difficulty in squatting. On bending , knee touches same side axilla. What is the probable diagnosis:

[AIPGMEE 2012]

A. SCFE

B. Perthe's d/s

C. Neglected DDH

D. Transient synovitis of hip

(Ans. A. SCFE)

SCFE (Slipped capital femoral epiphysis), epiphysis is displaced on femur neck and leg comes to lie in shortened and externally rotated position. Peak incidence is related to the start of puberty. Patient is unable to bear weight.

NOTES

PRENATAL AND PERINATAL FACTORS AFFECTING FETUS

Drugs taken during pregnancy and fetal effects/ teratogenic drugs :

● Anti-epileptics

- Phenytoin -- **Fetal hydantoin syndrome**
(microcephaly, cleft palate/ lip, hypoplastic phalanges, IUGR, neuroblastoma, bleeding d/to vit. K deficiency)
- Carbamazepine -- Spina bifida, ? NTD
- Phenobarbitone -- Relatively safe
- Valproate: -- Neural tube defects (NTD),

● Hormonal agents & related drugs

- **Synthetic progestins** -- Masculinization of female fetus, Hypospadias in male fetus, acceleration of fetal bone age
- **DES** -- In female offspring
Vaginal adenosis, T-shaped uterine cavity, septate Cx (at birth)
Incompetent os, Clear-cell vaginal adenocarcinoma in teenagers (at ~15-20 yrs)
-- In male offspring
↑ risk of testicular cancer in later life.
- **OCPs use & withdrawal** -- Limb reduction deformity
VACTERL association
(Vertebral, anal, cardiac, tracheo-esophageal, renal, limb anomalies)
- Clomiphene -- NTD, multiple births, Down's syndrome
- Prednisolone -- Oral clefts

● Drugs of abuse/ psychoactive drugs

- BZD (Diazepam) -- Cleft palate/ lip, withdrawal effect

- Alcoholism

-- **Fetal alcohol syndrome**

IUGR, microcephaly, facial dysmorphism/flat face (maxillary hypoplasia, small philtrum, ptosis, strabismus, ear anomaly, etc.), hemangiomas, autism, ADHD (Attention deficit hyperkinetic disorder), skeletal, cardiac (ASD > VSD) and other anomalies, **mental subnormality**
postnatal mental/ physical growth retardation, short stature (↓ length, wt, ht), borderline to severe MR

- Cocaine

-- Abruptio placentae, **preterm labour**, cerebral infarction

- Heroin

-- Irritability, hyperactivity, tremors, poor concentration in infancy

- Smoking

-- LBW (d/to underperfusion), IUGR/ SFD babies, ↑ risk of stillbirth, placenta previa, abruptio placentae, cleft lip/ palate, mental retardation, ↑ level of CO in maternal blood [functional inactivation of maternal & fetal Hb]

- LSD

-- "Fractured chromosomes" anomaly in fetus

- Amphetamine

-- IUGR, CHD, withdrawal symptoms

● Anticoagulants

- Dicumarol,

-- IUD, severe bleeding in neonate its derivative coumarin

- Warfarin

-- Birth defects, abortion, **hypoplasia of nasal bones**, stippled epiphyseal calcification resembling chondrodysplasia punctata, IUGR [CNS abnormality are reported if 2nd/3rd trimester exposure]

- *Other drugs*

- ACE inhibitors -- Renal tubular dysgenesis, lung hypoplasia, anuria, oligohydramnios
- Misoprostol (prostaglandin) -- Orthogryposis, cranial neuropathy (**Mobius syndrome**)
- Lithium -- Cardiac malformation (Ebstein anomaly), fetal goiter
- Mercury poisoning -- Causes **Minamata d/s** Japan (microcephaly and cerebral palsy)
- Thalidomide -- Phocomelia (long bone defects / limb reduction anomaly)
- Vit. K (synthetic) -- Hemolysis, hepatotoxicity severe neonatal jaundice
- Vit. D -- Vitamin D hypersensitivity syndrome/**William syndrome** Infantile hypercalcemia + Elfin facies + *Supravalvular aortic stenosis*
- Vitamin A analogues (Isotretinoin/ accutane) -- **Accutane embryopathy** NTD, renal/ craniofacial/ ear/ cardiac anomalies
- Thiazides -- Inhibit megakaryocytes (fetal thrombocytopenia, liver damage)
- Tetracycline -- **Cataract**, hypoplasia of enamel, pigmentation of teeth
- Chloroquine -- Relatively safe, may cause deafness
- Quinine -- Abortion, thrombocytopenia, deafness
- Streptomycin -- Deafness

→ *Most vulnerable period for organogenesis is b/w 18-55 days of gestation (in first trimester)*

→ *If teratogenic drugs are taken after 55 days -- developmental and functional abnormalities may result*

→ *Cessation of smoking during pregnancy has been shown to result in ↑ birth weight*

→ *Mobius syndrome is caused by maternal use of misoprostol, cocaine & thalidomide.*

→ *Cleft lip/palate c/by --- Diazepam, imipramine, phenytoin,*

→ *Maternal intake of salicylates (aspirin), thiazides, quinine, is a/w neonatal bleeding*

→ *Maternal intake of drugs of addiction e.g. morphine, pethidine, diazepam, alcohol, barbiturates results in "withdrawal syndrome" in neonate.*

Drugs taken by mother during perinatal period & imp. effects on neonate

- Oxytocin (used for induction in mother) -- Hyperbilirubinemia in girl babies
- Prolonged cortisone -- Adrenal crisis in infants
- NSAIDs -- Premature closure of ductus
- Dexamethasone -- Periventricular leucomalacia

Medications to the baby

- Chloramphenicol -- **Gray baby syndrome**
- Erythromycin -- Pyloric stenosis
- Vitamin K -- Bleeding, hepatotoxicity; severe NNHB

→ *Drugs ↑ing severity of hyperbilirubinemia & precipitating kernicterus in newborn -- Large doses of synthetic vitamin K (Kenendione), sulfonamides, salicylates, caffeine, novobiocin, gentamycin*

→ *Phenobarbitone induces maturation of UDP glucuronyl transferase & γ-acceptor protein & thus protects the baby from development of severe jaundice*

Category of Drugs taken during Pregnancy

Category		Examples
A	No fetal risk	
B	No fetal risk is demonstrated in animal or human studies	Pen, cephalo, Erythro, Clinda, Rmp, Ethm, Nitro, Ritonavir, saquin, AMB, praziquantel, piperacillin
C	Not adequate human studies	
D	Some evidence of fetal risk	Tetracycline, strepto, Tobra, Metro (1st trim.)
E	Proven fetal risk, Contraindicated	Quinine

Maternal disorder & fetal outcome

Maternal d/s	Outcome
• Bronchial asthma	No fetal risk
• Chronic cardiac d/s	Fetal goitre & hypothyroidism (effect of drugs, β ₂ agonis)
• Hypertension	Placental vasculopathy, IUGR
• Thyroid disorders	TSH does not cross placental barrier but LATS & HTSI antibodies can cross. Maternal hypothyroidism may result in congenital hypothyroidism
• SLE	Fetal death, IUGR, anti-phospholipid antibody & anti-Ro in 1/3rd (specific for neonates), Congenital complete heart block may be seen in neonatal lupus

Infant of a diabetic mother (IDM)

- DM is the commonest endocrine disorder met during pregnancy
- DOC for control of DM during pregnancy is insulin [oral hypoglycemics are contraindicated]
- Maternal high blood glucose level is reflected in the fetus as hyperplasia of the islet cells of pancreas. Positive anabolic effects of excess insulin results in fetal macrosomia, septal hypertrophy and cardiomegaly. **1st day hypoglycemia** is m/c manifestation. Hypoglycemia develops in 25% of babies but only small % babies become symptomatic.
- Baby is usually LGA. Macrosomia & organomegaly are seen [but size of adrenals & kidney is not affected]
- level of **glycosylated Hb (Hb_{1AC})** in the maternal serum is directly related to incidence of congenital malformations in 1st trimester & fetal macrosomia in 3rd trimester.
- Estimation of **Phosphatidyl glycerol** in amniotic fluid is the most reliable test to assess fetal lung maturity in mothers with DM
- Large, plethoric (polycythemia⁺) & moon face, hypertrichosis are seen. Hairy pinna is pathognomonic
- M/c complication during vaginal delivery in a diabetic women → Shoulder dystocia d/to fat deposition over shoulders.
- Sacral agenesis/ caudal regression are characteristic & CVS anomalies are m/c cong. anomalies.
VSD & HCM with asymmetric septal hypertrophy are common CVS defects. Cardiomegaly is seen in 30% of cases
- Other findings- hypocalcemia, hypomagnesemia, hyperbilirubinemia hypoglycemia, , HOCM, Hairy pinna, High RBC mass (polycythemia) [Remember with 7'H']
- There is increased incidence of HMD, monilial vaginitis seen in infants of diabetic mother

→ Estimation of glycosylated hemoglobin (**HbA1c**) reflects glycemic control over the previous 2-3 months. Overall risk of fetal congenital malformations are more if HbA1c value rise to $\geq 9.5\%$

→ Estimation of fructosamine reflects the glycemic control for the previous 2 to 4 weeks.

→ Estimation of GSA (glycosylated s. albumin) is a sensitive indicator for short term glycemic control.

→ Maternal serum **AFP** at 16 wks & a detailed high-resolution **USG** of the fetus including **ECHO** at 20-22 weeks are useful for detection of fetal anomaly in second trimester.

INTRAUTERINE INFECTIONS & OUTCOME

HBV

- HBV is usually transmitted at the time of birth during passage through birth canal & rarely transmitted in utero.
- Commonly results in carrier state. 60- 90% of affected newborn become chronic carrier of HBV (↑ risk of cirrhosis & cancer later in life) or it may cause severe hepatitis of infancy.
- M/m of newborns born to HBS Ag +ve mother:-
All neonates born to HBS Ag +ve mother should be given → HBIG (hepatitis B immunoglobulins) 0.5 ml i.m. + active immunization with HB vaccine 0.5ml i/m at separate sites preferably within 12 hours of delivery
- Risk of fetal transmission after maternal exposure to HBV**

	HBs Ag	HBe Ag	Risk of transmission
- In first trimester	+	-	10%
- In third trimester	+	-	5-10%
- At the time of delivery	+	+	> 90%

RUBELLA

- Fetal transmission is max^m if mother is infected in 6-8 wks of pregnancy.
- C/c of rubella are most likely to develop in first trimester of pregnancy (**50% in 1st month**, 20% in 2nd month and 8% in 3rd month).

CHICKEN POX (VZV)

- VZV infection during the early pregnancy (first 20 weeks) leads to → Spontaneous abortions and *fetal varicella syndrome* (LBW, cicatricial skin rashes, limb hypoplasia, eye findings). Virus affects DRG satellite cells.
- Max^m transmission (>24%) occurs in last month of pregnancy, which results in *congenital or neonatal varicella*.

SYPHILIS

- Treponema can cross placenta at any time in pregnancy but usually do not attack the fetus before 16 wks d/to +nce of Langhans cell layer.
- Fetal infection can even occur in the first trimester but b/ of fetal immuno-incompetence, the pathological changes are not observed in the fetus before 5th month.
- Rate of transmission is max^m (50%) if mother is suffering from **secondary syphilis**.

- Risk of spontaneous abortion is max^m when infection is acquired during 1st trimester

E.g. CMV, Rubella, VZV, HSV

- Risk of fetal malformations is max^m when infection is acquired during the period of organogenesis (b/w 3rd - 8th week or 18 - 55 days)

- Micro-organisms which can cause congenital malformations --- TORCHS, V (VZV)

- Micro-organisms which can cross placenta but do not cause congenital malformations --- Plasmodium, HIV, HBV.

- The risk for congenital infection is more when maternal infection occurs in third trimester

E.g. VZV, Toxoplasmosis, HBV

- Infections, of which max^m transmission occur near term or during passage of baby through birth canal..

Herpes, HBV, HIV (3 'H')

Recurrent fetal infections

- Seen with → VZV, CMV, syphilis, genital herpes (HSV-II) etc.
- Rare/ not seen with → Rubella

- CMV: preexisting maternal antibodies against CMV do not prevent reactivation or recurrent infection in pregnancy.

- Primary herpes simplex infection but not recurrent genital herpes in early pregnancy is a/w an rate of spontaneous abortions (50%) whereas in later pregnancy it manifests as stillbirth, prematurity and IUGR.

→ Commonest congenital infection is --- CMV (but it is usually asymptomatic)

→ M/c congenital infection a/w fetal malformations is --- Rubella

Classic triad in congenital ---

- RUBELLA

Deafness (m/c manifestation) + cataract + mental retardation

- SYPHILIS

Deafness (SNHL) + interstitial keratitis + Hutchinson's teeth (notched central incisors) & mulberry molars. Also k/as Hutchinson's triad

- TOXOPLASMOSIS

Chorioretinitis + intracranial calcification + hydrocephalus.

Infection	IUGR/HSM	Jaundice	Purpura	Eye D/g	D/g	CNS/other
CMV	60-70%	67%	67%	'Cottage cheese + ketchup/sauce' type peripheral chorioretinitis		Microcephaly Periventricular calcification
Rubella	60%	60-70%	67%	'Salt & pepper' chorioretinitis central type, involves macula		SNHL > PDA > Cataract. Deafness is the m/c manifestation. Microcephaly, M/R Periventricular calcification, Blue berry muffin rash CHD—PDA, PS also seen
Toxoplasma	20-30%	30-40%	30-40%	Central chorioretinitis (involves macula)	Double sandwich IgM ELISA IgM immuno sorbant assay	Hydrocephalus, multiple/ diffuse cerebral calcification (soap bubble calcification) [mnemonic hydro in toxo] Spiramycin is used to prevent maternofetal transmission
Syphilis	Rare	30-40%	Rare	Interstitial keratitis (salt and pepper fundus)		

TOXOPLASMOSIS

- Infants born to mother with toxoplasmosis usually (80-90%) do not have overt cl/ signs at birth.
- Toxoplasma in pregnancy with 4 fold rise in IgG titre indicates recently acquired infection but the results can be misleading unless IgM testing is done. Interpretation of serology.

Ig G	IgM	Interpretation
-	Equivocal	Possible early acute infection
Equivocal	+	Possible acute infection
+	-	Infected with toxoplasma >12 mo.
+	Equivocal	Probably infected with toxoplasma >12 mo.
+	+	Recent infection with toxoplasma <12 mo.

→ *M/c congenital infection a/w CNS calcification--- CMV > toxoplasmosis, herpes simplex.*

→ *Recurrent abortions are a/w genetic /chromosomal anomalies, m/c autosomy 16, TORCH infections etc.*

→ *Fetal malformations are not caused by maternal infections --- HIV, HBV, Pox, malaria, etc.*

→ *Recurrent abortions and IUGR are usually not seen in --- Syphilis*

→ *Sabin fieldman dye test is used to detect IgG in toxoplasmosis.*

PERINATAL TUBERCULOSIS

- True congenital tuberculosis is rare. Congenital TB in a neonate is acquired by transplacental transmission through a lesion in placenta or ingestion of an infected liquor.
- Under RNTCP, **sputum examination** is the preferred method for diagnosis of pulmonary TB.
- Use of Isoniazid, Rifampicin, Ethambutol, Pyrazinamide, Streptomycin, Kanamycin and Cycloserine has been considered safe for breast feeding, but safety of PAS is unproven.
- Postnatal TB is more common. Commonest mode of acquiring infection is ---from an open infectious case usually mother
- Transplacental transfer m/c affects liver. Hepatomegaly is the usual manifestation.

M/m of neonate born to mother having infectious TB

Neonates born to mothers having infectious TB should be given chemoprophylaxis with INH for 3 months or till the mother becomes noninfectious. BCG vaccination may be postponed or done with INH-resistant BCG vaccine. After 3 months

a) if mother has a negative sputum smear and the neonate (with a normal chest skiagram) has a negative MT→ Discontinue INH.

b) In case, the MT is +ve → a thorough search should be made for locating the presence of pulmonary or extrapulmonary focus and administration of ATT may be decided accordingly.

- Pulmonary TB in pregnancy is a/w incidence of preterm deliveries, LBW, and IUGR. Perinatal mortality is ↑ 10 fold. Cat I ATT has to be started immediately keeping in mind adverse outcomes. Ethambutol should be used in place of streptomycin. INH, Rmp, Pzm are safe to use in pregnancy.

PERINATAL HIV

- M/c mode of transmission is intrapartum transmission** (74-86% in India). It occurs d/to direct contact during delivery with maternal blood & genital secretions containing HIV.

- HIV transmission **efficiency** rates or efficacy

Type of exposure	Efficacy of single exposure
BT	> 95%
Vertical (transplacental)	> 30%
Breast milk	14-20%

- HIV is transmitted through breastmilk (max^m in first 5 months of lactation). Breastfeeding is contraindicated and replacement feeding is recommended. However in Indian scenario (or in developing countries) breast feeding is allowed under various recommendations.
- Mixed feeding (breast milk + trophic feed) carries maximum risk of HIV transmission.
- Methods of prevention of vertical transmission of HIV from mother to fetus:*

- Zidovudine to mother (in first trimester, during labour & after delivery). **Alternatively Nevirapine 200mg single oral dose** to the mother within 72 hours of labour (first stage) and single dose to newborn in a dose of 2 mg/ kg within 72 hours of birth has been found more effective. Efficacy is 47%
- Vaginal douches with povidone iodine.
- Elective cesarean section.
- Avoid ARM during labour.

Advanced age of mother (> 35 yrs) is related to high incidence of

- Down's syndrome
- Mental subnormality
- Premature labour
- Edward syndrome
- Dizygotic twins
- CNS defects [Mnemonic : DoMPED MOM]

Advanced paternal age (>50 year) is a/w increased incidence of

- Marfan's syndrome.
 - Achondroplasia
 - Craniostenosis with syndactyly (Apert's syndrome)
 - Down's syndrome with fusion of chromosome 21 & 22.
 - Osteogenesis imperfecta
 - Congenital deafness and some CHDs
- [Mnemonic : MAC DOC papa]

Antenatal predictors of chromosomal disorders

- Down's syndrome : ↑ Nuchal fold thickness, Reduced FL on USG, ↑ maternal serum hCG + PAPP-A
- Patau's syndrome : holoporencephaly, Cleft lip/ palate, echogenic kidney, polydactyly, Rocker bottom feet
- Edward's (Trisomy 18) : Spina bifida, Cerebellar agenesis, radial aplasia, single umbilical artery, club foot
- Diagnostic test for CDA type II --- HEMPAS
- ↑ Nuchal fold thickness combined with ↑ maternal serum hCG + PAPP-A --- Down syndrome
- Giantoblast are seen in --- CDA type III

NEONATOLOGY

Five cleans of Intranatal Care

- Clean hands
- Clean delivery surface
- Clean blade
- Clean tie (for cord)
- Clean cord

AAP-AHA 2010 NRP Guidelines

- Initial steps do not include giving supplemental oxygen. If cyanosis persists despite free flow oxygen give PPV. positive pressure ventilation.

- Routine intrapartum oropharyngeal and nasopharyngeal suctioning of babies born through meconium stained liquor no longer advisable.

• For term babies:

- Use of 100% oxygen is recommended when baby is cyanotic or when positive pressure ventilation is required during neonatal resuscitation.
- In situations where supplementary oxygen is not readily available positive pressure ventilation should be started with room air.

- Emphasis is on use of pulse oxymeter monitoring in labour room. Target SpO₂ for both term and preterm babies:

1 min	60-65%
2 min	65-70%
3 min	70-75%
4 min	75-80%
5 min	80-85%
10 min	85-95%

• For preterm babies:

- Begin PPV with oxygen concentration between room air and 30- 90% oxygen.
- Increase oxygen concentration up or down to achieve saturation between 90 and 95%.
- If HR does not respond by increasing rapidly to >100 per minute correct any ventilation problem and use 100% oxygen.

• Regarding PPV

- LMA should not be used
 1. In the setting of meconium stained amniotic fluid
 2. When chest compression is required
 3. In VLBW babies
 4. For delivery of medications

- Naloxone need not to be given by ET route. Epinephrine preferably by intravenous route only.

- Capnography (exhaled CO₂) recommended method of confirming tube placement. This may have no role in brief period of intubation for clearing meconium from trachea.

- After 10 minutes of continuous and adequate efforts if there are no signs of life (no heart rate and no respiratory effort) discontinue of resuscitative efforts.

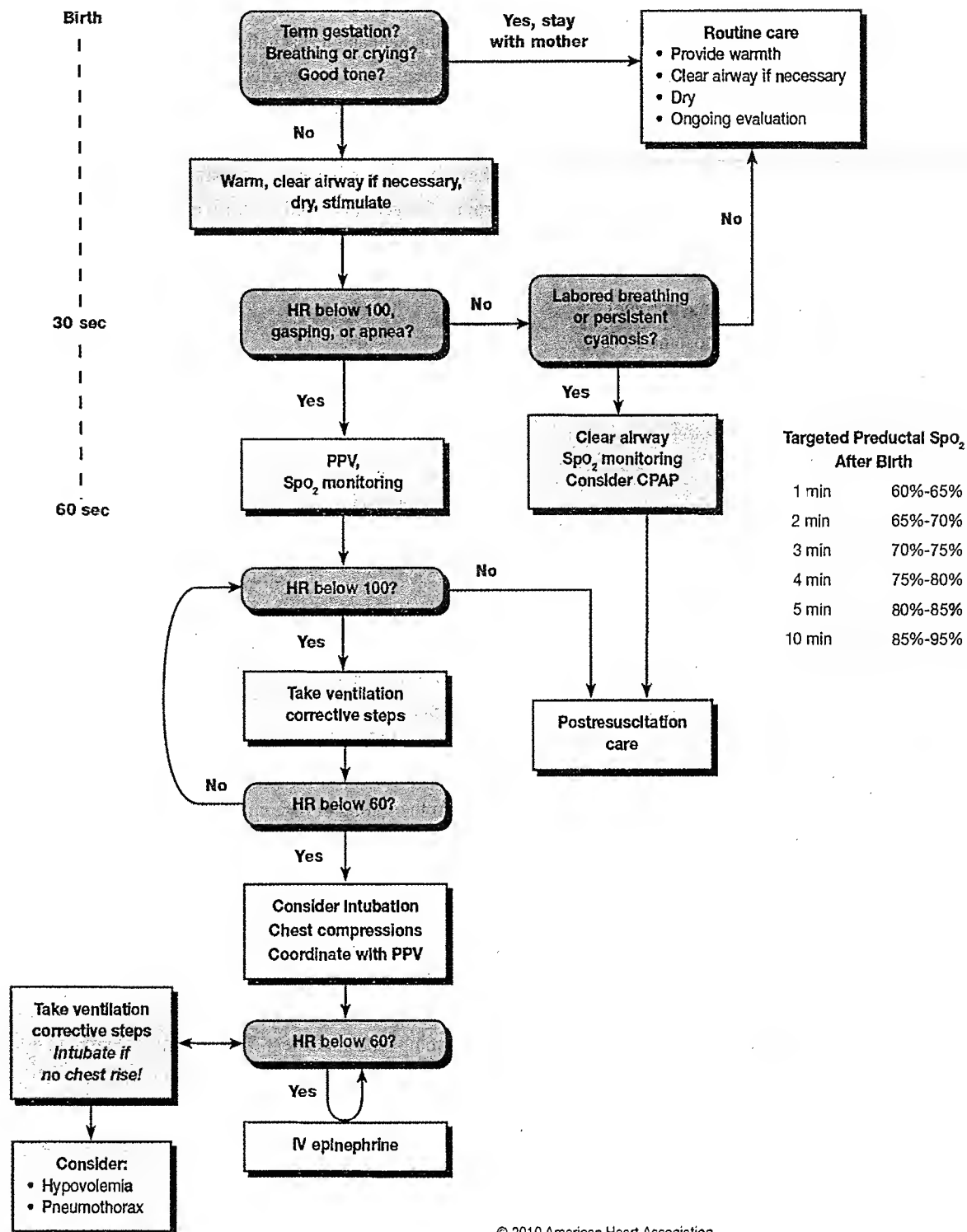
• Do not resuscitate (DNR) if

- When gestation, birth weight or congenital anomalies are a/w almost certain death (class IIa)
- Anencephaly
- Chromosomal anomalies incompatible with life e.g. trisomy 13

Neonatal Resuscitation Algorithm

(Courtesy : Adopted from AHA & NRP)

Newborn Resuscitation



© 2010 American Heart Association

Neonatal Resuscitation

Baby born with MSL (Meconium stained liquor)

- Newborn baby born with MSL may be classified as vigorous or non-vigorous.
- Vigorous baby is one who has strong respiratory efforts, good m/s tone, HR > 100 (APGAR is usually 8,9,9 at 1,5, 10 minutes respectively). Resuscitation is not required in these babies. Cleaning the baby of meconium and stomach wash is advised.
- Non-vigorous baby is one who is limp/ depressed at birth and has poor respiratory efforts/muscle tone/ HR < 100 (APGAR is usually 5-6 at 1 min). Immediate laryngoscopic tracheal suction. Tracheal suctioning and clearing of airway can be done under direct laryngoscopic visualization using large bore suction catheter (FG 12 or 10). ETT intubation may not be required in most of the cases. Stomach wash is advised.

APGAR Score

APGAR score is a quantitative method for assessing the infant's respiratory, circulatory and neurological status. It includes 5 criteria

A - Appearance (colour)

P - Pulse rate (Actually it is HR)

G - Grimace (response to catheter in the nose)

A - Activity (muscle tone)

R - Respiratory efforts

Score	0	1	2
1. Respiratory Effort	none	slow, irregular	good, crying
2. Heart rate (bpm)	Absent	< 100	> 100
3. Colour of the body	Blue or pale	Body pink extremities blue	pink
4. Muscle tone	flaccid	Some flexion the extremities	Actively moving
5. Reflex stimulation	No response	Grimace or sneeze	cries, coughs

[Remember that respiratory rate is **not** included in APGAR score]

- A normal baby will get a score 8-10, one min after birth. In asphyxia score is < 7
- Depressed neonate (Apgar score < 7) usually improves in response to O₂ by hood/ facemask, with or without PPV of lungs

- Tracheal intubation and perhaps external cardiac massage are indicated when Apgar is less than 3
- Any apnea at birth should be treated as secondary apnea. Secondary apnea is a/w fall in BP, and HR also begins to fall

No need to resuscitate if newborn is

- Full term
- Crying or breathing
- Has good muscle tone

Indication of BMV (Bag & mask ventilation) at birth

- Apnea at birth
- HR < 100 /mt, gasping baby

Contraindication of BMV

- Diaphragmatic hernia (Air pressure in GIT can worsen the situation)
- Meconium aspiration (Air pressure can push the particulate matter in distal airways → atelectasis /MAS)

→ In these situations endotracheal intubation is preferred

→ Tracheo-esophageal fistula is a relative contraindication

- Medications are indicated if RR remaining < 60 even after 30 sec. of assisted ventilation with 100% O₂ & an additional 30 seconds of ventilation accompanied by chest compression.

Drugs which can be given intratracheally during CPR

- Adrenaline
- Naloxone
- Lignocaine
- Atropine

→ NRP does not recommend use of Naloxone, lignocaine & atropine via ET route in neonates.

→ There is no role of sodium bicarbonate in neonatal resuscitation

→ Use of sodium bicarbonate has been found to have increased risk of IVH, hyponatremia, pulmonary hemorrhage in preterms

→ Mag sulph given to treat eclampsia in mother may cause neonatal hypotonia. To reverse its effect Ca-gluconate c/b given in neonate.

UMBILICAL CORD

- Usually cord is cut at 2-3 cm from the umbilical base.
- Contains **2 artery and 1 vein** (*Remember with the age old funda – left is left and right disappears*)
- Single umbilical artery*
 - It is a/w renal /genitourinary anomalies (m/c association), CVS anomalies, esophageal atresia and tracheo-esophageal fistula, imperforate anus
 - Incidence is 1%
 - A/w DM, prematurity, asphyxia.

Cord clamping

- Early cord clamping is done in*
Prematurity, Rh-incompatibility, birth asphyxia, IUGR, Baby of diabetic mother
- Delayed cord clamping is done in*
Postmaturity and cord around neck
- Cord care: Triple dye* (brilliant green, proflavine hemisulfate, and crystal violet) was considered one of the most effective agents (gold standard) for bacteriocidal prophylaxis, particularly for *S. aureus* of cord. Now a days no local application is advised.
- Cord blood is useful for*
 - Estimation of TSH, T_3 & T_4 . In screening of congenital hypothyroidism (TSH levels of $> 50 \mu\text{U/ml}$ in cord blood are diagnostic of neonatal hypothyroidism)
 - Screening of inborn error of metabolism / for tandem mass spectroscopy (TMS) e.g. in PKU, cystic fibrosis, G6PD deficiency
 - Sampling of an infant born to Rh-ve mother : for study of blood group, Rh type, s.bilirubin, coomb's test.
 - Prservation of fetal blood
- Cord is useful for*
 - Preservation of stem cells

Separation(Fall or closure) of cord

- On an average umbilical cord falls b/w 10-14 days.
- Delayed separation of cord is seen in*
 - Lack of LAM (Leucocyte Adhesion molecule).
 - Factor XIII deficiency
 - Immunodeficiency (Combined or CIDS)
 - antiseptics to the stump
 - Infection
 - Caesarean section
- Early separation of cord is seen in*
Trauma, pull

NEONATAL SEPSIS

- Early onset sepsis* occurs within 72 hours of life and is caused by organisms prevalent in the maternal genital tract or in the labour room. GBS are the m/c organism (while *Klebsiella*, *E.coli* and *S. aureus* are m/c in India).
- Late onset sepsis* is a nosocomial infection acquired from the nursery or lying in ward and occurs ≥ 72 hour after birth. Gram negative bacilli are m/c organism.
- Sepsis screen includes** (Usually ≥ 2 markers are taken significant)
 - ANC < 1000
 - Leucopenia $< 5000/\text{mm}^3$
 - Band cell to neutrophil ratio or I:T ratio (immature to total polymorphs) > 0.2 (band cells $> 20\%$)
 - CRP $> 8 \mu\text{g/ml}$ is +ve,
 - Micro ESR $> 15 \text{ mm/ first hours}$
 - Presence of $> 5 \text{ PMN/hpf}$ in gastric aspirate (limited utility in MSL, or blood stained liquor)
- Other markers of sepsis are--- **procalcitonin** and cytokines

→ Blood culture is confirmatory

→ leucocytosis $> 20,000$ is not predictive of newborn infection because TLC of 20000 on D_1 and upto 27000 on D_2 are considered normal in a neonate

→ *Listeria* infection may produce preterm delivery, intrauterine diarrhea and MAS.

→ Early conjugated NNHB with direct bilirubin $> 0.5 \text{ mg/dL}$ is noted in neonatal sepsis

→ Persistent NNHB with direct bilirubin $> 20\%$ of total bilirubin and pale stools suggest cholestatic jaundice which is usually noted 2-4 weeks after birth.

HIE

- Initial response to hypoxia is \uparrow CBF d/to redistribution of cardiac output by the 'diving reflex' and rise in BP. Cerebral edema aggravates HIE.
- Status marmoratus** is seen in Kernicterus and is d/to basal ganglia defect.
- In preterm babies deeper vessels are deficient and hence they develop periventricular ischemia and leukomalacia which leads to spastic diplegia. Disability is more in LL (In term babies there is more superficial cortical ischemia and disability is more in UL)
- Sarnat & Sarnat staging** is used for staging HIE in stage I, II and III. This staging is useful only for babies over 36 weeks

Large for date (LGA) babies are a/w

- Constitutional (m/c cause)
- TGA, hydrops
- Beckwith Widman syndrome
- Soto syndrome/ Cerebral gigantism
- Marsh syndrome
- Maternal DM or prediabetes (gestational diabetes), hypo/ hyperthyroidism
- Cretinism

Term Babies

- Suffer more **cortical ischemia** and infarcts which may lead to multifocal necrosis, porencephalic cyst, hydronephaly

PRETERM BABIES

- o Can tolerate hypoxia for longer period without sequelae
- o Suffer more **periventricular ischemia** as cortical vessels are more superficial
- o PVL (Periventricular leukomalacia) and CP without seizures.
- o Hypoglycemia is d/to impaired gluconeogenesis

Risk of	Preterm	Term
Brain ischemia	Periventricular	Cortical
PVL	More	less
CP	Without seizures	With seizures
PDA	More	-
Apneic spells	More	-
Sepsis	More	Less
ROP, BPD	+	-

Prematurity+ oxygen toxicity predisposes to

- o Retinopathy of prematurity (Retrolental fibroplasia)
- o Bronchopulmonary dysplasia (BPD), CLD (Chronic lung d/s)

Antenatal steroid therapy (ANS)

- o Is a/w ↓ incidence of → RDS or HMD, IVH, NEC [Mnemonic: RIN]
- o Is a/w improved maturity of skin and thus reduced insensible water loss
- o Optimum effect is seen if delivery expected: after 24 hour and <7 day after starting ANS therapy.
- o Lancet trials have shown that multiple doses of antenatal steroids though reduce the incidence of HMD but are a/w long term CNS complications like CP, PVE & neuronal damage.

- o Effects are better in female fetus & better with betamethasone.

Postnatal corticosteroids

- o Postnatal steroids are not recommended because of chances of poor neuro-developmental outcome. **No role** in m/m of HIE, sepsis, meningitis & MAS.
- o Some therapeutic utility in m/m of sclerema neonatorum.

Vitamin E

- o Role in prevention of BPD, ROP (bec/ of its anti-oxidant property) and hemolytic anemia in neonate and prevention of preeclampsia in mother.
- o Excess of vitamin E is a/w ICH (intracranial h'age) & NEC.

→ As compared to term SFD babies (term IUGR), preterm neonates are at higher risk of - PDA, RDS HMD, Apneic spells, NEC, IVH, Sepsis & Hypothermia [Mnemonic: PRANISH]

→ Most of the newborn pass urine by 12 hrs of age & almost all of them do so by 48 hr.

→ Most of newborn pass meconium by 24 hr. If a newborn does not pass meconium by 24 hours or urine by 48 hours it is a matter of concern.

→ Fetal adrenal cortex is largest organ of fetus (compared to adult size), its size is ~85% of adult size in fetus.

→ M/c manifestation of acute hypoxemia in a newborn --- Bradycardia, cardiac asystole.

Physical criteria of Preterm & Term

Criteria	Preterm	Term
Sole creases	Anterior 2/3 only	Extensive
Breast nodule	< 5 mm	5-10 mm
Ear cartilage	Thin, Poor recoil fine, wooly	Thick, Good recoil thick, silky
Hairs	fine, wooly, lanugo, abundant	thick, silky
Genitalia	Testes undescended, hypopigmented rugae (Labia separated in females)	Testis descended, pigmented rugae (Labia majora completely covers labia minora)

- o New (modified) Ballard score is includes neuro-muscular

maturity as criteria for gestational age assessment. Ranges from -1 to +4.

Retinopathy of Prematurity

- Premature newborn should not be placed in incubator with an O_2 concentration of $>30\%$.
- Percentage of oxygen which can be safely given to preterm in order to prevent ROP is $<60\%$.
- All preterm babies born ≤ 32 weeks of age and those weighing 1500g or less should be screened for ROP.
- The first examination by indirect ophthalmoscopy should be done b/w 6-7 weeks post-natal age or 34 weeks post-conceptual age (whichever is earlier).

ROP screening criteria

- All infants born at ≤ 32 weeks
- All infants with birth weight < 1500 grams
- Very sick babies who required ventilatory support, multiple BT.

Further m/m is :

Grade	Labelling of retina	T/t
I	Mature (vessels have reached within one disc diameter of both nasal and temporal ora- serratae)	Does not require t/t →further follow up
II	Immature (vessels are short of one disc diameter of the nasal or temporal ora- serratae but ROP is not developed yet)	Require weekly follow up
III	ROP	
	Stage 1, 2 (Usually resolve spontaneously in 80-90% cases)	Require weekly examination
	Stage 3 (threshold d/s)	Cryo or laser
	Stage 4	Cryo/laser + scleral buckling
	Stage 4b and 5	Vitrectomy
	Stage 5 (Complete RD)	Vitrectomy

- **Plus d/s** is c/by vascular dilatation and tortuosity of the posterior retinal vessels and indicates severe degree of progressive ROP.
- **Pre-threshold d/s** is divided into 2 types
High risk type Type I : require laser photocoagulation
(In zone 1 any stage + /stage 3 in zone II stage 2/3+)
Low risk type Type II : require weekly/bi-weekly observation
(In zone 1 stage 1/2 – and stage 3 – in zone II)
- **Threshold d/s** is stage 3+ ROP in zone I or 2 occupying at least 5 contiguous clock-hours or 8 non contiguous clock-hours of retina. T/t is laser photocoagulation.

- Anti-oxidants (vit E) & slow reduction in O_2 has no role in established ROP.

IUGRS/SGA Babies

Feature	Malnourished SGA	Hypoplastic SGA
1. Timing when affected during gestation	Later part (3rd trimester)	Early part of gestation
2. Cause	Placental dysfunc ^a	Teratogens, infections, genetic / chromosomal diseases.
3. Pattern of IUGR	Asymmetrical IUGR	Symmetrical IUGR
4. HC	≥ 3 cm + CC	
5. PI (Ponderal index)	< 2	> 2

- In **Mixed SGA babies** adverse influence of early + late gestation are reflected. Hypoplastic + Malnourished mixed picture is seen.

Fetal monitoring

- **Fetal scalp blood pH** is the best method to assess fetal hypoxia. fetal scalp pH < 7.15 is a/w asphyxia.
- OCT is not used now-a-days. Only NST is used--- if NST is non-reassuring decision is taken to deliver the baby.

Neonatal reflexes

Reflex	Onset	Disappearance
Moro	birth	3 months
Stepping, placing (automatic walking)	"	1.5 mo
Sucking, rooting	"	4-7 mo
Palmar grasp	"	4-6 mo
Plantar grasp	"	10 mo
TNR	"	2-3 mo
Landau's	3 mo	24 mo
Parachute reflex	9 mo	Persists throughout life

Moro's reflex

- Moro's reflex is a vestibular reflex
- 3 phases - Abduction Extension Adduction
- It appears at 28-30 wks of gestation (but lacks adduction

component i.e. incomplete) and completed by 38 wks and disappears by 3-4 months of age.

- Reflex is less extensive in ---- Hypertonia & HIE stage I
Difficult to illicit in ----- Severe hypotonia, extreme preterm babies
Depressed / reduced in ----- maternal sedation, cerebral depression / damage
Increased or Jumpy / exaggerated ----- In cerebral irritability
Asymmetrical in ----- Erb's palsy, # clavicle/ humerus or a hemiplegia
- At 28-32 weeks of gestation, Moro's reflex appears and it persists for 3 months of age when Landau's reflex appears which persist for 9 months of age, at 9 mths parachute reflex appears which persists throughout the life.
- Sucking & swallowing become coordinated only after 34 wks of gestation
- **Primitive reflexes that reappear in CNS disorders are---**
Grasp reflex, palmo-mental reflex, glabellar tap, snout reflex & sucking reflex.
- Palmar grasp is present at birth & disappear at 4-6 mo. of age. Plantar grasp may persist up to 10 months of age.
- Pincer grasp is attained at 10 months of age.
- **TNR (Tonic neck reflex)**
 - Asymmetric TNR is present at birth, well developed at 1 month, and disappears at 6-7 month
 - Symmetric TNR (cat's reflex) develops at 4 months of age, disappears at 8-12 month
- Galant's reflex is trunk incurvation reflex.
- Abnormal persistence of symmetric & asymmetric TNR beyond 6-9 month of age indicates spastic cerebral palsy. This will make the baby 'locked in the fencer's position.
- Babinski's sign may persist up to 2 yrs. of age till myelination is complete but in practice, flexor response is noted in many normal newborns & infants. Babinski sign indicates hemiplegia
- Startle reflex is elicited by sudden loud noise or by tapping the sternum ----- elbow is flexed (not extended, as in Moro's) and hand remains closed.

Common neonatal problems of no significance (normal abnormalities of neonate)

- Mastitis neonatorum
- Vaginal discharge (pseudo menses)
- Caput succedaneum
- Erythema toxicum

- Sub conjunctival h'age
- Mongolian spots
- Milia, Epstein pearls

NEONATAL SEIZURES

- Hypocalcemia is the m/c biochemical abnormality causing seizures in neonates. Prognosis of hypocalcemic seizures is excellent. T/t is i.v. calcium gluconate, which is given slowly under cardiac monitoring.
- M/c type of seizures seen in newborn are subtle seizures. GTCS are rare
- DOC for neonatal seizures is **phenobarbitone**. Other useful drugs are ---midazolam, lorazepam, phenytoin, etc.
- Pyridoxine deficiency is also a/w neonatal seizures.

Choanal Atresia

- D/to persistence of bucconasal membrane.
- Should be ruled out at birth.
- u/L choanal atresia is asymptomatic and may get undetected at birth.
- b/L choanal atresia is incompatible with life if untreated. Cyanosis and respiratory distress seen with feeding and improves with crying (opening of mouth) is the hallmark of b/L choanal atresia.

CYANOSIS

- Appears when oxygen saturation is < 85% and level of reduced Hb levels is high (> 5 gm%).
- Cyanosis in a newborn baby may be central or peripheral. Peripheral cyanosis will improve with warmth and improved oxygenation.
- *Central cyanosis is due to cardiac, respiratory, CNS or hematological causes.*
 - ➔ *Hyperoxia test is useful in differentiating cyanosis d/ to cardiac and respiratory d/s. Administration of 100% oxygen leads to rise of PaO₂ above 150 mmHg rules out a cardiac disease.*
 - ➔ *Cyanosis occurring with first feed (or excessive frothing and chocking) --- suggest the diagnosis of tracheoesophageal fistula.*
 - ➔ *Cyanosis and respiratory distress esp. with feeding and improves with crying (opening of mouth) → suggests the diagnosis of B/L choanal atresia.*
 - ➔ *U/L choanal atresia is usually asymptomatic or may go undetected.*
 - ➔ *Cyanosis precipitated by crying/ straining in infants or older children → suggests tetralogy of Fallot (TOF) or rarely other cyanotic CHDs. Spells are k/ as hypercyanotic/ blue or tet spells.*
 - ➔ *High position of larynx in an infant enables him to suckle and breathe (use of nasal airway) at the same time.*

D/d of Respiratory distress in newborn

Properties	HMD	MAS	TTN
Onset	< 6 hrs	First few hrs	first 24 hrs
Risk Factor	Prematurity, GDM	MSL, listeriosis, post maturity, fetal distress, IU asphyxia	Term LSCS, Male
CXR	Ground glass appearance/ white washed lung, Air bronchogram	Coarse granular opacities, air trapping/ emphysema, hyperinflation	Prominent vascular marking, Fluid in interlobar fissure
Complicane	↓↓↓	↓	
Resistance	No change	↑↑↑	

→ MAS is usually seen in fetal distress and postmaturity. However in Listeriosis fetal diarrhoea may lead to preterm deliver with MSL.

→ PROM, fever in mother, foul smelling liquor, h/o sepsis / UTI pneumonia, chorioamnionitis, unexplained preterm labour are risk factors for congenital pneumonia in a baby.

Transient Tachypnea of the Newborn (TTN)

- Also k/as **type II RDS** or **wet lung syndrome**
- Common among term babies born by cesarian section .
- Other risk factors are: Precipitate delivery, delayed cord clamping, macrosomia, maternal sedation, prolonged labour with administration of large amount of IV fluids to mother. (conditions a/w fluid overload)
- Onset of tachypnea few hours after birth with minimal evidence of respiratory distress
- On CXR :Hyperinflated lung field, Line as streaking at hila d/to dilated lymphatics,
Interlobar fluid with minimal effusion, prominent vascular markings and prominent interlobar fissure.

Neonatal Hyperbilirubinemia (NNHB)

- Kernicterus is common in Crigler Najjar syndrome .
- ABO incompatibility is the m/c cause of physiological jaundice now a days as ABOi is more common than Rhi.
- Essential investigations in a baby delivered to Rh-ve mother : DCT, PS for hemolysis, baby blood group, Retics, S. bilirubin (T & D), Hb.

Important Causes

Onset of jaundice	Causes
< 24 hour (Day1)	<ul style="list-style-type: none"> Hemolytic ds of newborn (m/c cause) ABO (more common) Rh-incompatibility (more severe) Intra-uterine infections Deficiency of G-6-PD, Pyruvate kinase, hexokinase Homozygous-α-thalassemia Lucy - driscoll syndrome Drugs to mother e.g. vit. K Hereditary spherocytosis Crigler-Najjar Synd
b/n 24-72 hr	Physiological jaundice precipitated & prolonged by hypoxia, hypothermia, hypoglycemia, prematurity, polycythemia, cretinism, high altitude etc.
b/n 72 hr - 2 wk	<ul style="list-style-type: none"> Septicemia (m/c cause) Neonatal hepatitis. EHBA. Breast milk jaundice (BMJ) Metabolic d/s Galactosemia, α-AT def, tyrosinemia Cystic fibrosis. IHPS, intestinal obstrucⁿ

- Clinical jaundice in the first 24 hours of life is always pathological. Other features of pathological jaundice are :-

- STB > 15 mg/dL (STB = Serum total bilirubin)
- STB \uparrow se is > 0.2 mg% /hr or > 5 mg% /day
- Direct serum bilirubin is > 15% of STB or > 2 mg%
- Clinical jaundice persisting beyond 2 weeks

Prolonged unconjugated NNHB

- Suspected when clinical jaundice persists beyond 10 days in term & > 14 days in preterm
- Causes : Immaturity, HDN, BMJ, hypothyroidism, pyloric stenosis/ intestinal stasis, concealed h'mge (as in cephalhematoma), malaria, Criglar Najjar syndrome

Prolonged conjugated NNHB

- Rare condition.
- D/s usually noticed first time after 3 weeks or 18 days
- Causes: idiopathic neonatal hepatitis, infections, inspissated bile syndrome, malformations(EHBA, Zellweger, Alagile's syndrome etc.), metabolic d/s, TPN, chromosomal disorders

- Exaggeration of physiological jaundice is seen in ABO incompatibility.
- No t/t is required for physiological jaundice. Increased breast feeding is advised.
- Breast milk Jaundice (BMJ) :**
 - Prolonged unconjugated hyperbilirubinemia
 - Develops after 3 days & may persist for 2 months at times.
 - Hepatic conjugation of bilirubin is compromised d/to presence of 3- α 20- β pregnanediol. Babies pass colorless urine & golden yellow stools
- M/m of NNHB in healthy term baby : TSB & Phototherapy & Exchange transfusion cut off

Age in hours	Consider photo-therapy	Photo-therapy	EBT if intense photo-therapy fails	EBT + intense phototherapy
< 24	-	-	-	-
25-48	> 12	< 15	> 20	> 25
48-72	> 15	> 18	> 25	> 30
> 71	> 17	> 20	> 25	> 30

Phototherapy

- Phototherapy is indicated in general when bilirubin $\geq 15\text{mg/dl}$ (or 10mg/dl in preterm)
- Phototherapy leads to photo-oxidation and photoisomerization (**e-isomerization**) of bilirubin (lumirubin) and thus helps in excretion
- Phototherapy uses blue light in spectrum of 450-460 nm wavelength & an irradiance of 6-12 microwatt/ cm^2/nm . Narrow spectral fluorescent blue light tubes, with peak output at 425- 475 nm, is most effective
- Intense phototherapy** is recommended for 'higher risk' babies. It uses high level of irradiance in the 430-490 nm band ($\geq 30\text{ microwatt/ cm}^2/\text{nm}$)
- A decline in bilirubin of at least 0.5 to 1 mg\%/hr is expected in initial 4-8 hours
- C/c :** increased water loss, loose greenish stools/ diarrhoea, flea beaten rashes on trunk, cold stress, retinal damage.
- Phototherapy is mainly effective in unconjugated NNHB. If phototherapy is given to a baby with direct(conjugated) NNHB, bronze pigmentation of baby results (bronze baby syndrome)
- Congenital porphyria or a family history of porphyria is an absolute contraindication to phototherapy.

Exchange Transfusion (EBT)

- Early EBT** is indicated in Rh HDN if
 - Cord Hb $\leq 10\text{ gm\%}$
 - Cord bilirubin $\geq 5\text{mg\%}$
 - Rate of s. bilirubin increase is $>0.5\text{mg\% per hour}$

- Subsequent EBT** is indicated if

Age (in hours)	TSB (total s. bilirubin)
<24	>10
25-48	>15
>48	>20

Choice of blood for EBT

Situation	In emergency situation	Ideal to use
Rh isoimmunization	O Rh - ve RBCs	O Rh -ve blood suspended in AB plasma
ABO incompatibility	O Rh types baby (Rh compatible with baby)	O Rh types baby suspended in AB plasma
In other situation	cross matched with bay's blood	

- Blood volume required is ---160- 180 ml/ kg in double volume EBT.
- C/c of EBT:** thrombocytopenia, portal vein thrombosis, NEC, dyseleotroemia, sepsis, air embolism, death.
 - When conjugated bilirubin is $> 20\%$ of the total bilirubin it is called direct (conjugated) hyperbilirubinemia
 - Serum bilirubin: protein ratio > 3.5 is a/w higher risk of brain damage
 - Bilirubin staining characteristically involve: Basal ganglia, hippocampus dentate, inf olivary, subthalamic nuclei, auditory nuclei in kernicterus.
 - Drugs reducing bilirubin in neonate when given to mother --- phenytoin, barbiturates, aspirin
 - Drugs promoting jaundice within 24 hrs (by displacing bilirubin)---Vit K, salicylates, sulfonamides
 - In Rh-ve mothers, two doses of anti-D globulin (300 μg) may be administered i.m.. First prophylactic dose at 28-32 weeks of pregnancy and then 2nd dose at birth (within 72 hours of delivery/ abortion/ MTP) to prevent Rh-sensitization.
 - 1 gram of Hb yield 35 mg of bilirubin.
 - 1 gram of albumin binds equimolar bilirubin= 8.5 mg of bilirubin.

- There is some role of Fibre optic blankets, Tin metalloporphyrins, albumin transfusion in t/t of NNHB
- Phenobarb** c/b used for priming for hepatobiliary scan in cholestatic jaundice, suspected Crigler najjar syndrome and following EBT in hemolytic settings where need for repeat exchange is anticipated.

BREAST FEEDING

Comparison b/w human milk, cow milk & colostrum

	Human/ Breast milk	Cow milk	Colostrum
Protein	↓ (1.1g)	↑ (3.5g)	↑↑
Fat	↓	↓	
Lactose	↑ (6.5g)	↑ (6.5g)	↓
Vitamins	C (60 mg), D(50 IU)	C (20 mg), D(25 IU)	A and D
Minerals.	Iron	Na ⁺ , Cl ⁻ , K ⁺ , Ca ⁺⁺ , Mg ⁺⁺	Na ⁺ Cl ⁻ , Mg ⁺⁺
↑ Ca ⁺⁺ / PO ₄ ratio	>2	Ca ⁺⁺ , Mg ⁺⁺ >2	
Immunoglobulins	IgG, IgA, IgM	Rich in IgG, IgA, IgM	
Other	Whey proteins, β-casein (ratio of 80: 20)	lactoglobulin, α-casein	

- Fore milk**
Rich in **proteins**, lactose sugar, vitamins, minerals & water.
- Hind milk**
Rich in **fat** and provides energy
- Preterm milk**
Rich in fat, protein, Na⁺, calories (Low lactose / CBH)
- Transitional milk**
Milk secreted b/w day 3 to 2 wk.
(Mature milk is secreted after 2 weeks)
- Breast fed babies are less likely to develop*
 - Eczema and mik allergy (because allergens, α-casein, lactoglobulins are absent in human milk)
 - Obesity, hypertension, DM & atherosclerosis in later life
 - Late-onset tetany, metabolic acidosis, and acrodermatitis enteropathica are limited to top fed babies
 - No risk of infective diarrhoea
 - Low incidence of RTI, acute otitis media, NEC

- Human beta casomorphin & NGF promotes neurodevelopment.
- Lactoferrin** is bacteriostatic & inhibits E. coli. It promotes absorption of iron, zinc & Mg.
- Bifidus factor** promotes growth of lactobacilli.
- BSSL** (Bile salt stimulated lipase) kills amoeba and Giardia & **PABA** present in breast milk is important in protection against malaria.
- Lactation helps in involution of uterus & ↓ PPH.
- Breast milk secretion is maximum at 5-6 months of age. Daily output is aprox. 600 ml/d

→ Human milk is a good source of vitamins except vitamin K.

So breast-fed infants are more susceptible to HDN d/to vit.K deficiency.

→ Breast feeding is inadequate for preterm and VLBW babies

→ Human milk is rich in amino acid glutamic acid and deficient in glycine

→ Feeding advise for HIV +ve mother---Exclusive breast feeding followed by early abrupt weaning or replacement/ complimentary feeding (But mix feeding is **not** recommended)

Storage of Milk

Unrefrigerated breast milk should be used within one hour of expression. Refrigerated milk c/b used within 48 hours of expression

Re-freezing of thawed frozen milk should not be done

Contraindication to breast feeding

- Galactosemia, mother with active TB, HIV in developed countries, mother on cytotoxic or certain other drugs
- HBs Ag + ve mother, HCV, CMV, fever in mother, tobacco smoking are **not** contraindications to breast feeding

Milk secretion

- PROLACTIN** is the hormone which promotes secretion of milk in lactating women (*milk secretion reflex*)
- OXYTOCIN** is the hormone responsible for ejection or release of milk in lactating women, which acts by contracting myoepithelial cells (*milk ejection reflex*)
- Suckling* of infant at breast is the stimulus required to initiate **let down reflex** which is maintained by oxytocin

NUTRITION

Malnutrition/ PEM

Indicators of malnutrition

1. Weight

Simplest, most widely used & reliable indicator of MN. Weight is measured using a beam scale/salter type scale.

2. Height

Measured by stadiometer. Length is measured by infantometer in lying down posture for infants.

3. Other indicators

MAC	→	< 12.5 (severe MN)
Triceps SFT	→	10-6 mm (mild), < 6 mm (mod-severe)
Quetelet index	→	< 0.14
Dugadole index	→	< 0.79

4. Age-independent indicators are :

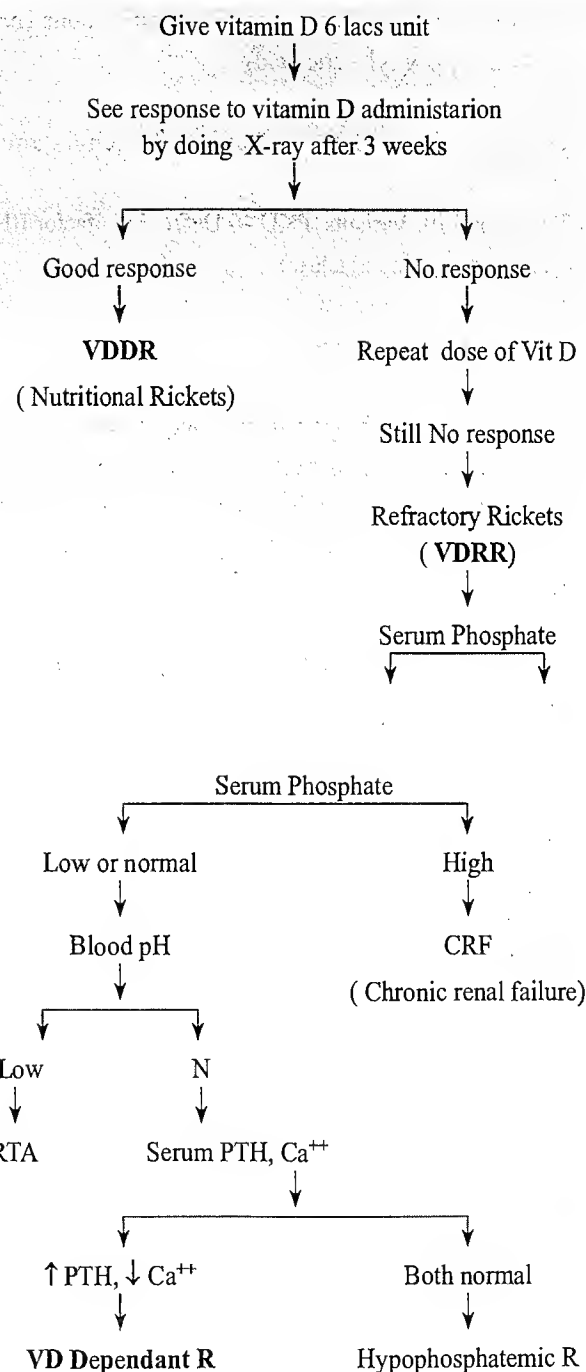
The Bangle test, Shakir tape, QUAC stick, BMI, MAC, MAC/HC (Kanawati Index)

- First indicator of PEM is → low W/A (includes both acute and chronic malnutrition)
IAP classification of PEM is based on → W/A (> 80% of expected is considered normal)
- Wasting** (low W/ H, < 80%) --- signifies acute malnutrition
- Stunting or shortness** (low H/A , < 90%) --- Signifies chronic malnutrition.(duration of MN)
- Wasting and Stunting both** --- Signifies acute on chronic malnutrition
- Nutritional dwarfism**
Normal birth weight with subsequent retardation (W/A and H/A are low, but W/H may be normal), delayed bone age
- Predictors of increased mortality in MN ---low s. albumin (< 2.1 mg/dl), low serum total lipids and phospholipids
- Marasmus** is c/by --- Old man appearance, wasting , weight <60% of expected, alert, good (voracious) appetite
- Kwashiorkor** is c/by --- Edema, moon face, weight 60- 80 % of expected, apathic (altered mentation), hepatomegaly d/to fatty liver, poor appetite, low levels of insulin, 'Flag' sign in hairs
- Pellagra** is characterized by 3 'D'
Diarrhoea +
Dementia +
Dermatitis (Castle necklace)

→ Three type of dermatosis is seen in Kwashiorkor---Enamel paint type, Flaky paint type, Crazy pavement type

→ Apart from PEM Crazy pavement dermatosis is also seen in --- Ichthyosis & Pellagra.

Approach to a child with Rickets



METABOLIC DISORDERS

Phenylketonuria

- D/to deficiency of enzyme *phenylalanine hydroxylase* or its cofactor *BH4*
- AR disorder; defective gene is on 12q. H/o consanguinity in family may be present
- Classically manifests as 'blue eyed blonde' with mental retardation
- Persistent vomiting, eczematous skin rash, hyperactivity, athetosis, mousy/ musty odour (d/to presence of phenylacetic acid)
- Types :
Type I, Classic PKU --- Defect in phenylalanine hydroxylase
Type II and III, Variants PKU --- Defect in cofactor BH4 (dihydrobiopterin reductase)
Type III and IV, Variants PKU --- Defect in biosynthesis of cofactor dihydrobiopterin
- BH4 (Tetrahydro biopterin) deficiency presents with mental retardation, hyperalaninemia, myoclonic seizures
- *Screening test* is **Guthrie test** using bacillus subtilis (It is performed on blood sample 48-72 hours after protein feed). It is replaced by TMS (Tandem Mass Spectrometry) now a days.
- Lab d/g is based on emerald green colour with FeCl_3 test in urine
- T/t – Lifelong low phenylalanine diet. Tyrosine supplementation in diet as it becomes essential amino acid.
- Pregnant mothers with PKU are prone to give birth to babies with microcephaly, mental retardation and cardiac defects (VSD)
- Main aim for the first line therapy is to limiting the substrate for deficient enzyme

→ *Guthrie test can detect --- PKU, Galactosemia and MSUD*

Galactosemia

- AR disorder
- Classical galactosemia is d/to def. of *galactose-1-phosphatase*
- Accumulation of Gal-1-phosphate produces hepatotoxicity and mental retardation and galactitol (dulcitol) produces cataract.
- Other Cl/f – prolonged conjugated hyperbilirubinemia,

FTT, hepatosplenomegaly, vomiting, hypoglycemia, irritability, aminoaciduria, cirrhosis, ascites.

- Lab/f – Urine is +ve for reducing substance with Benedict's reagent and Clinitest but negative glucose oxidase test. Galactose is +ve in urine chromatography oxidase test
- T/t – Lactose free diet. Early dietary restriction of all type of milk.
Galactosemia d/to def. of *galactokinase* deficiency presents with galactosemia, galactosuria, and cataract without mental retardation

Hereditary fructose intolerance (HFI)

- Rare AR disorder d/to def. of *1-phosphofructoaldolase* (Fructose – 1 – phosphate accumulates)
- Symptoms of abdominal distension, bloating and flatulence start with honey/ table sugar as they contain fructose. Child avoids fruits and sweets
- HFI leads to liver damage
- Urine – RS and Clinitest +ve but Clinistix is negative
- Fructose H_2 breath test is diagnostic.

GROWTH & DEVELOPMENT

Growth in underfive children

Age	W/g (kg)	Length/Ht. (cm)	HC (cm)
Birth	3	50	33-35
3 month	5	60	39-40
6 month	7	66	42-44
9 month	9	71	44-45
12 month	10	75	45-47
2 year	12	87	47-49
3 year	14	94	49-50
4 year	16	100	50-51

- Most newborn loose wt. upto 10% initially in first 10 days regain in another 10 days, then wt gain is
200 gm/wk in first 3 months,
150 gm/wk in 3-6 months,
100 gm/wk in 6-12 months
- Wt velocity is 6 kg in the first year, 2 kg/yr. in preschool child (between 1-6 year) & 3 kg/yr in school going child (> 6 year upto puberty)
- Ht velocity is 25 cm in the first yr, 12.5 cm in the second year & 6 cm/yr. after 2 year till puberty.
After 2 years formula for calculation of height is = Age in years + 77 cm

Important Developmental Milestones

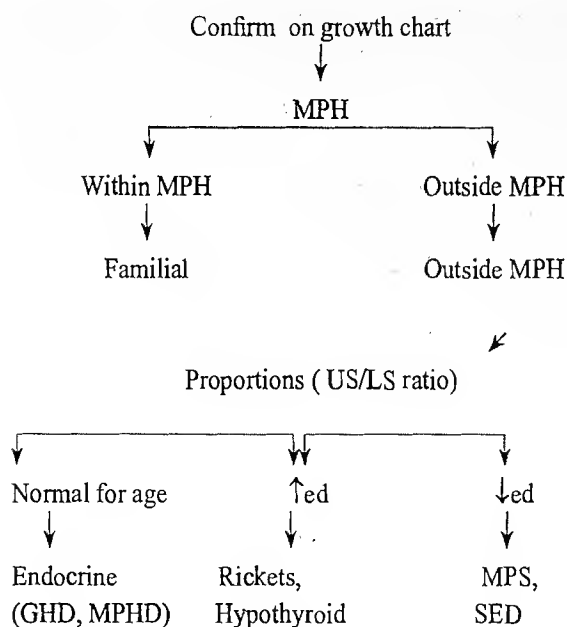
Age	Gross motor	Fine motor	Language	Personal & social
1 month	Turns head to sound	—	—	—
2 months	—	—	—	Social smile
3 months	Neck holding	—	cooing	Recognize mother
4 months	—	Grasp a rattle or ring when placed in hand	—	—
5 months	Sitting with support	Bidextrous grasp (holds object with both hands)	—	—
6 months	Roll over	—	Monosyllables (ma; ba)	smiles at mirror image
7 months	—	Palmer grasp	—	—
8 months	Sitting without support	—	—	Plays 'peek a boo',
9 months	Standing with support crawling	Pincer grasp seen (picks a pellet with thumb & index finger)	Bisyllables (dada, mama)	Waves bye-bye
10-11 mths	Walking with support, <i>cruising</i>	—	—	—
12 months	Standing alone/ without support	Pincer grasp matures	Two words with meaning 'bye'	Plays a simple ball game
13 months	Walking without support	—	—	—
18 months	Running with cup	Can feed himself with slight spilling	10 words with meaning	Almost dry by day
24 months	Walking upstairs	Draw a horizontal or vertical line	simple sentence	—
36 months	Riding tricycle Walking upstairs with alternative steps	Can draw a circle Can dress or undress himself	Telling a story	Knows gender (age, sex)

D/d of Short stature

	Constitutional	Familial	Hypopituitarism	Hypothyroidism	Turner syndrome
1. Family h/o SS	+	+	-	-	-
2. Birth wt & height	N	L	N	N	L
3. Growth pattern	Slow from early childhood	Slow from birth	Early in childhood	Slow from birth	Slow from birth
4. Growth velocity	Low N	N	N	Low	Low
5. Bone age	BA < CA by <2 yrs	BA = CA	BA < CA by >2 yrs		BA = CA
4. Epiphyseal development	Moderate	N	retardation	Severe retardation	Variable
5. Puberty	delayed	N	delayed	delayed	delayed
5. G.H. levels	N	N	L	N	Variable

- Baby is able to draw or copy a horizontal/ vertical line at 2 year(scribbles), circle by 3 years,a plus sign at 4 years, a multiplication sign at 5 year of age.
- Baby can imitate a rectangle by 4.5 yrs, a triangle by 5.5 yrs & a diamond by 6 years of age.
- An infant has bidextrous approach & uses both hands with equal preference. Hand preference in an infant may points towards hemiparesis. Handedness evolves by 2 yrs of age.
- By 1 year, baby can make a few steps. By 15 months, the baby can walk sideways/backward, run by 18 months. Baby can climb stairs with both feet per step by 24 months, can walk on tip toes by 30 months, climb stairs 1 foot per step & can climb down stairs with alternate feet by 36 months. Baby can skip (hop) by 5 years.

SHORT STATURE



GHD = GH deficiency

MPHD = Multiple Pituitary hormone deficiency

MPS = Mucopolysaccharoidosis

SED = Skeletal Dysplasia

MPH = Mid parental height

= (MHT + FHT -13) /2 for girls

= (MHT + FHT +13) /2 for boys

Condition	Relationship b/w growth parameters
Acute on chronic d/s	CA > HA > WA
Endocrine SS	CA > WA > HA
Precociuos puberty	HA > WA > CA
Constitutional delay	CA > BA = HA
Endocrine obesity	WA > HA > CA

[WA = Weight age, HA = Height age, CA = Chronologic age]

INFECTIONS

EBV and Infectious Mononucleosis

- Incubation period is 4-6 weeks
- No specific precautions or isolation procedures are recommended, since virus is found in the saliva of healthy people.
- Clinical diagnosis can be made from the characteristic triad of fever + pharyngitis + lymphadenopathy lasting for 1-4 weeks.
- Although the symptoms of IM resolve in 1-2 months, EBV remains dormant or latent in a few cells in the throat and blood for rest of the life.
- Serologic testing is method of choice for diagnosing primary infection. Serological tests include:
 1. Normal to moderately elevated TLC (10,000-20,000)
 2. Increased no. of lymphocytes (usually 2/3rd of TLCs)
 3. >10% should be atypical lymphocytes.
 4. Positive reaction to "monospot test"
- When "mono spot" or heterophile test are negative, additional lab tests are required to differentiate EBV infection from a mononucleosis like syndrome (caused by CMV, adenovirus, or Toxoplasma gondii)

These EBV specific lab tests are based on measurement of antibodies to several antigen complexes. These antigens are VCA (Viral capsid antigen), the early antigen, and the EBV nuclear antigen (EBNA).
- Antibody to EBNA appears after 4 weeks.
- T/t is symptomatic. No antiviral drugs or vaccines are available.
- Use of corticosteroids has been indicated for acute symptoms like impending airway obstruction, massive splenomegaly, myocarditis, hemolytic anemia. But published data is lacking.

- o Rash of IM is ↑ed by ampicillin.
- o Interpretation

	IgM Anti-VCA	IgG Anti-VCA	IgM Anti EA	Anti EBNA
1. Susceptible	-	-	-	-
2. Primary infection (Acute)	+	+	+/-	+/-
3. Past infection	-	+	+/-	+
4. Reactivation	-	-	+	+

ARI & Pneumonia : Classification and Drugs

Signs of symptoms	Classification	Recommended T/t by WHO	Where to treat
1. Cough/cold only	No pneumonia	Home remedies	Home
2. RR > 60 in <2mth >50 in 2-12 mth > 40 in 1-5 yr.	pneumonia	co-trimoxazole	Home
3. Chest indrawing	Severe pneumonia	IV/IM Penicillin	Hospital
4. Cyanosis, severe chest indrawing unable to drink	Very severe	IV chloramphenicol	Hospital

- Recommended drug for ARI in ARI control program: Co-trimoxazole.
- In infants <2 month only 2 classes. No pneumonia and severe pneumonia.

CVS

Causes of CCF

- o At birth --- Hypoplastic left heart syndrome, Severe TR/PR, large systemic AV fistula
- o In newborn period (0-3 d) --- Obstructive lesions MS, PS, AS
- o Onset b/w Day 4 - day 7 --- Hypoplastic heart, TAPVR

Teratogenic Drugs and CHD

- o Phenytoin induced --- PS, PDA, VSD, ASD, CoA
- o Lithium --- Ebstein anomaly

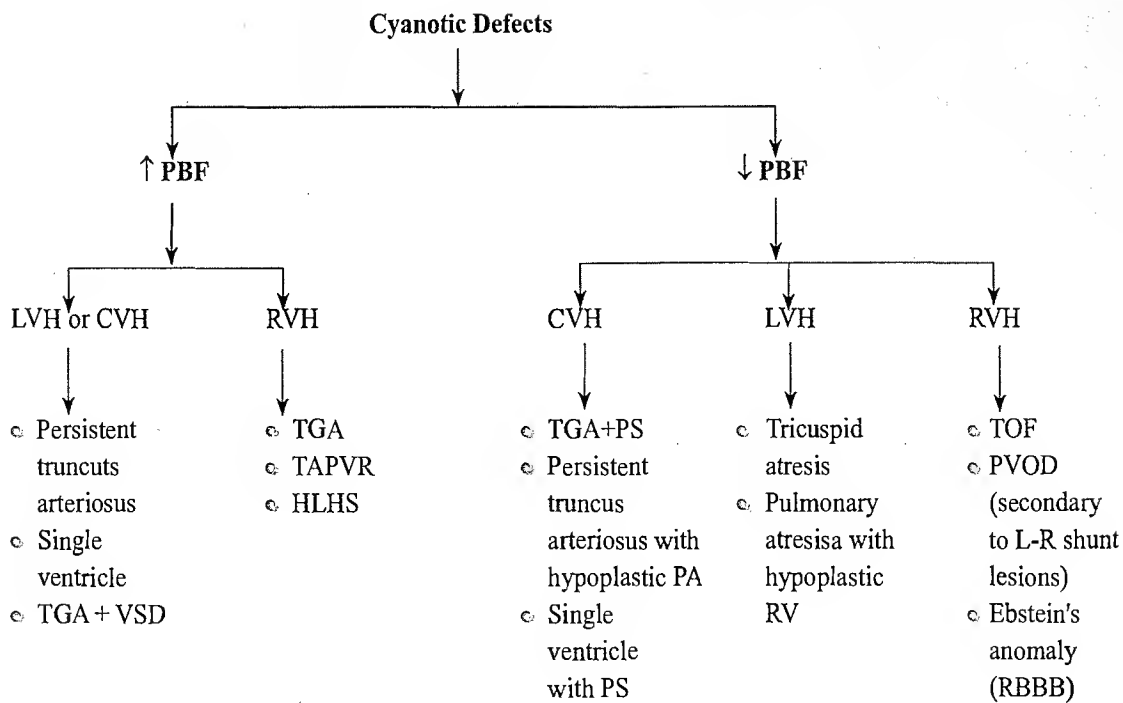
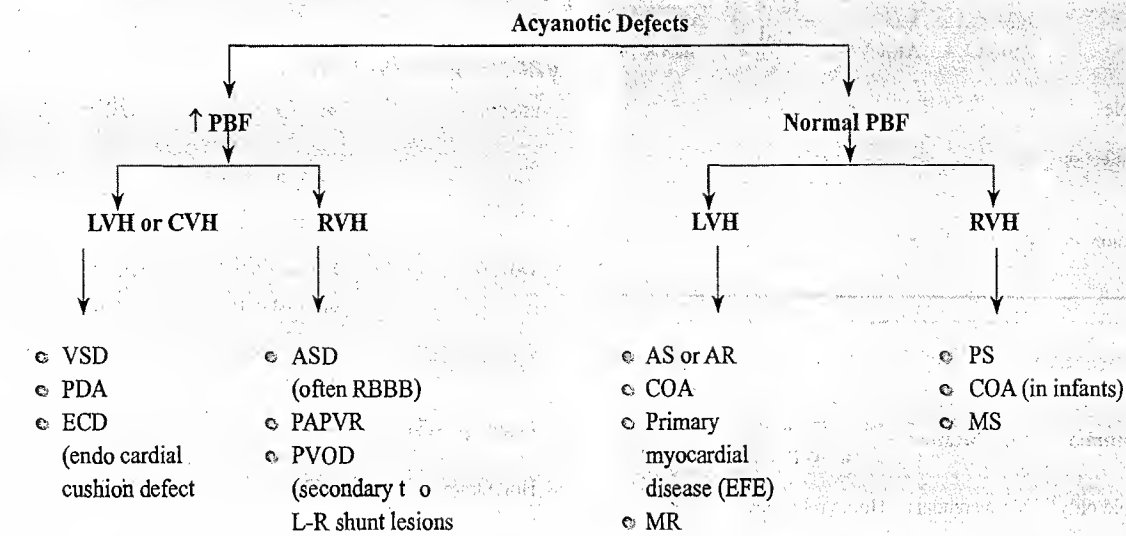
- o Alcoholism --- VSD, ASD
- o Retinoic acid --- Conotruncal anomalies
- o Valproate --- CoA, hypoplastic left heart

Syndromes a/w CHD

Syndromes	M/c CHD	Other defects
o Turner (44,XO)	CoA, bicuspid aortic valve	Eclipse burn
o Down's	Endocardial cushion defects	ASD (primum type)
o Edwards (tri-18)	VSD	
o Patau's (tri-13)	VSD	
o Holt Oram	ASD	VSD, 1° heart block
o Rubella	PDA	Peripheral PS
o Marfan's	AR	
o DiGeorge	VSD + interrupted aortic arch	
o Noonan's	Valvular PS	
o Allagile's	Peripheral PS	

- M/c type of ASD are secundum type (10 : 1) but in Down's syndrome primum ASD are more common
- In Noonan's syndrome, pulmonary stenosis is of infundibular type.
- In TOF pulmonary stenosis may be infundibular, valvular & subvalvular (but never supravalvular type).
- In William's syndrome, aortic stenosis is supravalvar type.
- Lutembacher's Syndrome is congenital ASD + acquired MS (usually rheumatic)
- Small heart is seen in --- Constrictive pericarditis, Addison's d/s, dehydration, cyanotic CHD, Malnutrition
- Infants of diabetic mother are likely to have --- VSD, asymmetric septal hypertrophy, cardiac anomalies

Congenital Heart Diseases (CHDs) Classification



Duct Independent lesion of Heart

Require urgent surgery :

- ☐ TAPVR
- ☐ Truncus arteriosus
- ☐ ALCAPA

Duct Dependent lesion of Heart

These lesions will worsen by infusion of PGE₁

- *Pulmonary flow is ductal dependent*
 - Critical PS with intact ventricular septum
 - Tricuspid atresia
 - TOF

- *Systemic flow is ductal dependent*
 - Congenital valvular AS
 - CoA
 - Interrupted aortic arch
 - HLHS (Hypoplastic left heart syndrome)
- *Oxygenation is ductal dependent*
 - TGV

Imp. Sporadic disorders

Association	Major CHD	Other
VATER Association		+ Vertebral anomaly Anal arteria, TE fistula, Radial, renal anomaly
VACTERL Association	VSD	+ VATER + Limb defect, 'C' for cardiac defect
CHARGE Association	TOF	+ Coloboma, Choanal atresia Retardation mental, growth Genital, Ear anomaly
William Syn.	Supravalvular AS	Elfin facies + Peripheral PS + Hypercalcemia

LT-TO-RIGHT SHUNT LESIONS

ASD

- Ostium secundum defect is **m/c** type (50 to 70%). The defect is located at the fossa ovalis. However in Down's syndrome, primum ASD is more common.
- MVP is a/w ostium secundum or sinus venosus defects in 20%.
- Usually asymptomatic
- **O/E** –
 - Thin slender built
 - **Widely split and fixed S₂** and a grade 2- 3/6 systolic ejection murmur.
- **ECG** – Right axis deviation of +90 to +180, mild RVH and a 'rsR' pattern in V₁ are typical.
- **CXR** – Cardiomegaly with enlargement of RA & RV, ↑ PBF
- Infective endocarditis does **not** occur in patients with isolated ASDs. Prophylaxis for IE is not indicated unless ASD is a/w MVP.
- Spontaneous closure of the secundum defects have occurred in about 40% of patients in the first 4 yr of life.
- M/m: Non-surgical / device closure : Clamshell and Amplatzer device are available. Pulmonary to systemic blood flow ratio (Qp : Qs) of $\geq 1.5:1$ indicates the need for surgical closure.

VSD

- VSD is the **m/c** form of congenital heart defect and accounts for 15% to 20% of all such defects.
- Perimembranous defects are **m/c** type (70%)
- The "swiss cheese" type of multiple muscular (trabecular) defects are extremely difficult to close surgically.
- An infundibular defect may produce AR and cause an obstruction in the right ventricular out flow tract
- **CI/f**
 - With a *small VSD*, patient is usually asymptomatic with normal growth and development
 - *Moderate to large VSD* produce delayed growth, ↓ exercise tolerance, repeated pulmonary infections and CHF are common during infancy.
 - With long standing pulmonary HTN, a H/o cyanosis and a ↓ level of activity may be present.
- **O/E**
 - Infant with large VSDs may have poor weight gain or show signs of CHF
 - Cyanosis + clubbing may be present in patients with pulmonary vascular obstructive disease (**Eisenmenger's syndrome**)
 - Systolic thrill may be present at the lower left sternal border (precordial bulge and hyperactivity are present with a large shunt VSD)
 - The intensity of P₂ is normal with small shunt and moderately ↑ ed with a large shunt.
 - The S2 is loud and single in patients with pulmonary vascular obstructive disease. A grade 2- 5/6 regurgitant systolic murmur is audible at lower left sternal border.
- **ECG** – LVH and occasional LAH in moderately VSD, Large VSD may cause CVH with or without LAH
- **CXR** – Cardiomegaly involving LA, LV and sometimes RV.
- In pulmonary vascular obstructive disease the main PA and the hilar vessels enlarge noticeably. Heart size usually normal.

Natural history

- Spontaneous closure occurs in 30 to 40% of patients with membranous and muscular VSDs during 1st 6 months

- CHF may develop after 6 to 8 weeks of age in infants with large VSD
- Pulmonary vascular obstructive disease may begin to develop as early as 6 to 12 months of age in patients with large VSDs, but the resulting right to left shunt usually does not develop until the teenage years.
- M/m ---T/t of CHF, if develops, is indicated with diuretics and digoxin for 2-4 months. Non-surgical / device closure is possible for selected muscular VSDs using 'Umbrella' device (experimental stage)

Eisenmenger Syndrome

- Patient has severe PAH (pulmonary arterial hypertension) resulting in R → L shunt at the ventricular or pulmonary artery level.
- On ECG there is Rt axis deviation d/to RVH, P pulmonale may be present.
- CXR shows prominent pulmonary arterial segment and oligemic lungs

Eisenmenger Complex

- Consist of PAH + VSD providing R → L shunt.
- Impending signs of PAH are --- palpable S2 /single S2, parasternal heave, murmur of functional PR (Graham steel's) along LLSB.

PDA

- There is persistence of ductus b/n the left PA and the descending aorta (5-10 mm distal to the origin of subclavian a.)

Cl/f

Patient is usually asymptomatic if ductus is small. A large shunt PDA may cause a LRTI, atelectasis and CHF

O/E

- Wide PP with **bounding pulses**. There is **CO₂ retention**, requirement of mechanical ventilation if pulm. pressure falls.
- Tachycardia and exertional dyspnea
- With pulmonary vascular obstructive ds, a right to left shunt results in Cyanosis only in the lower half of the body (i.e., differential cyanosis)
- The precordium is hyperactive, a systolic thrill may be present at the upper left sternal border.
- A continuous (machinery) murmur best audible at the left infraclavicular area or upper left sternal border.
- ECG – A normal ECG or LVH with small to moderate PDA. CVH with larger PDA
- CXR – Similar to VSD3

- Risk of pulmonary hemorrhage is there d/to increased PBF. PDA in preterm neonates is a/w NEC.

Natural history

- Unlike PDA in premature infants, spontaneous closure of a PDA does not usually occur in full term infants.
- CHF ± recurrent pneumonia develop if shunt is large
- SBE, more frequent with small PDA

M/m

- Indomethacin is ineffective in term infants with PDA and should not be used.
- Prophylaxis of SBE
- Non-surgical (catheter) closure by **Rashkind** PDA occlusion device (Stain Wils)
- Surgical – Anatomical existence of PDA, regardless of size, is an indication for Surgery. The presence of pulmonary vascular obstructive disease is a contraindication to surgery.

→ D/d of continuous murmur : Coronary/ systemic/ pulmonary AV fistula, VSD with AR, Ruptured sinus of valsalva

Complete TGA

- Prevalence is 5% M:F = 3.1
- In D-TGA the aorta arises anteriorly from RV carrying desaturated blood to the body and PA arises posteriorly from LV carrying oxygenated blood to lungs
- Defects that permit mixing of the 2 circulations (e.g. ASD, VSD & PDA are necessary for survival
- About half of these infants do not have associated defects other than a PO or a small PDA (i.e. simple TGA). In some of these subpulmonary stenosis occurs.
- Association – VSD (30-40%) COA, interrupted aortic arch, pulmonary atresia
- The classic complete TGA is called D-transposition in which aorta is located anteriorly and to the right (dextro) of the PA.
- Hx**
H/o cyanosis from birth is always present
Signs of CHF, dyspnea and feeding difficulties develop during the newborn period.
- O/E**
Moderate to severe cyanosis. If CHF supervenes, hepatomegaly and dyspnea
S₂ is single and loud, a systolic regurgitant murmur to VSD.
- Lab /f**
- Severe arterial hypoxemia with or without acidosis.

Hypoxemia does not respond to O₂ inhalation

- Hypoglycemia and hypocalcemia are occasionally present.
- o **ECG** – RVH, QRS axis is rightward
- o **CXR** – An egg shaped heart with narrow, superior mediastinum and ↑ PBF
- o **Natural history**
 - Progressive hypoxia and acidosis result in death
 - CHF develops in the first week of life and without surgical interventions death occurs in 90% of patient before they reach 6 months of age.
 - Infant with intact ventricular septum (Sickest group) response best to Rashkind balloon atrial septostomy.
 - Infant with VSD are the least cyanotic group but the most likely to develop CHF and pulmonary vascular obstructive disease.
- o **M/m**
 - Oxygenation
 - **Prostaglandin E₁ infusion** to improve arterial oxygen saturation
 - **Surgical**
Definitive repair that switch right and left sides blood at 3 levels and left sides blood at 3 levels
The atrial level – **Senning** or **Mustard** operation
The ventricular level – **Rastelli** operation
The great artery level – **Jatene** operation (arterial switch operation is procedure of choice)

TOF

- o TOF is the m/c cyanotic heart defect seen in children beyond infancy.
- o M/c symptom is DOE & exercise intolerance
- o It is the commonest congenital lesion in which squatting is noted
- o **Coer on sabot** on CX×R d/to absence of main pulmonary segment
- o Predominantly right to left shunt
- o D/to maldevelopment of the bulbous cordis

- o **Fallot's Tetralogy** → VSD + Mild PS
- o **Fallot's Trilogys** → PS + ASD or Patent Foramen ovale + RVH
- o **Fallot's tetralogy** → VSD (peri membranous) + Overriding of aorta + RVH + infundibular PS
- o **Fallot's Penitology** → Fallot's Tetralogy + ASD

History

- A heart murmur audible at birth
- Most patients are symptomatic b/n 6-12 months of age with cyanosis.
- Affected infants may present with CCF
- Cyanosis at birth is seen in cases with severe pulmonary stenosis and pulmonary atresia.
- Older children manifest with cyanosis, clubbing, polycythemia, hemoptysis and FTT. Exertional dyspnea and squatting are usual features.
- Frequent hyper cyanotic blue spells or 'tet' spells may occur during the first 2 years of life.

O/E

- A RV tap along left sternal border & a systolic thrill at the upper & mid-left sternal borders in 50%.
- An ejection click originating from aorta . **Single S₂** bec/ of only aortic component
- A long, loud (grade 3-5/6) ejection systolic murmur.

ECG –

Right axis deviation but in acyanotic form, the QRS axis is normal

CXR

- Heart size is **normal** or smaller
- Pulmonary **oligemia** (Black lung fields) are seen in TOF and PS
- **Boot shaped heart** or 'coeur en sabot'

Natural History

- Infants with acyanotic d/s gradually become cyanotic. **Polycythemia** develops secondary to cyanosis.
- Hypoxic spells may develop in infants
- Coagulopathy is a late C/c
- Brain abscess & CVA, SBE
- o **M/m of hypoxic spell**
 - Knee-chest position in infants
 - Morphine, O₂, NaHCO₃, Phenylephrine, ketamine, propranolol

Oral propranolol for prophylaxis against hypoxic spells

Surgical

1. **Classic Blalock-Taussing** shunt (b/n SCA & PA ipsilateral)
2. **Waterson** shunt b/n ascending aorta & the right PA. Pott's shunt b/w descending aorta and left pulmonary a.
3. Infants with TA & normally related great arteries survive beyond 6 months of age without surgical palliation.

M/m – Indomethacin, Rustelli operation

Tricuspid Atresia

- Accounts for 1-3% of CHDs
- The tricuspid valve is absent, and the RV is hypoplastic.
 - Associated defects like ASD, VSD, or PDA are necessary for survival
- In 50% of patients small VSD & PS is present. Other associations are ASD, TGA, CoA
- CI/f

Hx : Severe cyanosis since birth, tachypnea, poor feeding hypoxic spells

O/E : Cyanosis ± clubbing, single S₂

Occasionally a continuous murmur of PDA

- ECG : "Superior" QRS axis (b/n 0° and -90 degrees)
- CXR : Heart size is normal or slightly ↑, with RA & LV enlargement, PBF ↑es in most patients (but ↑PBF may be seen if a/w TGA).

Total Anomalous pulmonary venous return (TAPVC)

- Accounts for 1% of CHDs. Male preponderance.
- Supracardiac type (50%) is the m/c. The common pulm. venous sinus drains into rt SVC through left vertical vein and the left innominate vein.
- An inter-atrial communication (ASD or PFO) is necessary for survival. PFO occurs in 70% of pt.
- CI/f : Depends upon pulmonary venous obstruction

	Without obstruction	With pulmonary venous obstruction
Hx	CHF, growth retardation, frequent pulmonary infection esp. with infracardiac type	Marked cyanosis & respiratory distress in neonate, cyanosis worsens with feeding
O/E	Precordial bulge, Hyperactive RV impulse, S ₂ widely split & fixed, P ₂ accentuated, Mid-diastolic rumble at lower left sternal border	Loud single S ₂ , Gallop rhythm, Crackles in lungs, Hepatomegaly
ECG	RVH (Volume overload type)	RVH
CXR	Cardiomegaly involving RA, RV, 'Snowman' or figure of 8 configuration	Heart size normal or slight ↑ Pulmonary edema

- Natural History: CHF & repeated pneumonias are common

- M/m

- Intensive anti-congestive measures with digitalis & diuretics
- All infants with pulmonary venous obstruction should be operated on soon after d/g

GIT, DIARRHEA AND DEHYDRATION

Concentrations of electrolytes in ORS

Ingredients per litre	Grams		Low osmolality /new ORS (mmol/L)	ReSoMal
NaCl	2.6 g	Na ⁺	75	45
KCl	1.5 g	K ⁺	20	40
Trisodium citrate	2.9 g	Cl ⁻	65	70
Glucose	13.5 g	Citrate	10	7
Water	1 lit.	Glucose	75	125
Osmolality			245	300

- Total osmolality is 245 mOsm/L (while in old ORS it was 310)
- This new formula ORS is helpful in reducing stool volume by 20%, incidence of vomiting by 30%, I.V. supplemental therapy by 33%. There is **low incidence of hyponatremia** compared to standard WHO- ORS.

→ Stool Na⁺ content in cholera → 90 mmol/L

→ Stool Na⁺ content in rota virus diarrhoea → 70 mmol/L

→ So the ideal replacement fluid should be based on Na⁺ lost in stools.

→ Bicarbonate is hygroscopic and does not remain in powder form so replaced by citrate now a days in new formula ORS.

→ Trisodium citrate was included in place of sodium bicarbonate b/c of better stability and shelf life of citrates and it is claimed to decrease stool output by 8-14%

→ WHO recommends the use of ReSoMal (Rehydration Solution for Severely Malnourished Child) for diarrhoea in children with malnutrition. This contains less sodium and more of potassium than the standard WHO ORS solution. It also contains Zn, Mg, and Cu. ReSoMal is given 70-100 ml/kg to restore normal hydration in 12 hrs.

→ In ORS glucose is used because it helps in absorption of sodium by cotransport mechanism.

Persistent Diarrhea

- Diarrhea that lasts ≥14 days
- PD is more common in malnourished infants and young children.
- Dietary m/m is the mainstay of t/t.

NEUROMUSCULAR SYSTEM

D/D OF ACUTE FLACCID PARALYSIS (AFP)

Feature	Polio	GBS	Traumatic neuritis	Transverse myelitis
Etio	Polio entero viruses I, II, III	Immune (delayed HS)	first 24 hrs	Unknown, ?viruses
Progress	in 24 - 48 hours	hours - 10 days	Hours - 4 days	Hours - 4 days
Fever	High, always present at onset	+/-	++	Rare
Sensory	No deficit, Backache, severe myalgia	Hypoesthesia of palm/soles, Cramps, tingling	Pain in gluteal region	Sensory loss in LL with sensory level
Paralysis	Assymetrical, proximal	Symmetrical, proximal	Asymmetrical, distal Affect only one limb	Symmetrical, involve LL
Tone	↓↓ (Global hypotonia, head lag)	↓ /-nt	↓ in LL, Paraparesis	-nt in LL in early phase
DTR	↓ /-nt	-nt	↓ /-nt	↑ (Hypereflexia) late sign
Bladder involvement	-	+/- (Transient)	-	+
Autonomic dysfunction	Dysautonomia	Sweating/flushing	Rare/-nt	-
EMG at 3 wk	Abnormal		Normal	Normal
CSF WBCs	↑	↑↑↑ (Albumino cytological dissociation)	↓ /Normal	↑ /Normal
CSF Protein	↑ /Normal	-	Normal	-

- AFP is defined as acute onset (<4 weeks) of flaccid paralysis in **any child <15 year of age** who has no obvious cause (severe trauma / electrolyte imbalances) for paralysis is found, or paralytic illness in a person of any age in which polio is suspected.
- Polio virus c/b found in faeces from 72 hours prior to onset of paralysis + upto 6 weeks or more after infection, with highest probability of virus isolation being during first 2 weeks after onset of paralysis.
- A case of AFP occurs every year for every 100,000 population of children aged <15 years (*background rate*)
- 2 stool samples** should be collected 24-48 hour apart within 14 days of onset of AFP for virus isolation. Or if AFP cases are seen late (i.e. >2 weeks) after onset of paralysis then stool specimens may be collected upto 60 days after onset of paralysis. At least 'one thumb sized' 8 gram of stool is

required which is stored at temp < 8°C

- Non polio-AFP rate** is an indicator of surveillance sensitivity. The NPAFP rate < 1/ 100,000 is the minimum expected no. of cases
- Maximum cases have been found in western UP
- Polio eradication** is--- absence of clinical cases of polio for at least 3 yrs & -nce of detectable wild viruses from community.

Other d/d of AFP

- Non polio enteroviruses, hypokalemia, peripheral neuropathies
 - Pseudoparalysis** : Electrolyte imbalance, Scurvy, Congenital syphilis, Osteomyelitis, RA, Trichinosis, Septic arthritis
- [Mnemonic - ESCORTS]

MUSCLE DYSTROPHIES

Type	Genetics	Age of onset (yr)	Involvement (girdle)	Progression	Remarks
Duchenne's	XR	2-5	Pelvic	Fast	Severe form, Pseudohypertrophy of calf m/s, subnormal intelligence
Becker's	XR	8-10	Pelvic	Slow	Mild form Pseudohypertrophy, pes cavus
Emergy Dreifuss	XR, AD	5-10	Biceps, triceps, peroneal ms	Slow	Arrhythmias, elbow contractures, humeral/peroneal m/s weakness, Deltoid spared.
Congenital MD	AR	Newborn	Generalised	Slow	Face mildly involved, diffuse hypotonia, arthrogryposis (AMC)
Facioscapulohumeral	AD	Adolescent	Face, shoulder, upper arm	-	Asymmetric, Winging scapula
Limb girdle	AR, AD	10-30	pelvic/shoulder	slow	Cl/f may be like DMD, or BDM
Myotonia congenita	AD/AR	2-3	generalised	slow	Pseudohypertrophy of calf

- Pseudohypertrophy of calf m/s is characteristic of **DMD** but c/b seen in Becker's, GSDs, myotonic MD, limb girdle MD, cysticercosis.
- After calf m/s next m/c site of hypertrophy in DMD is --- tongue
- **Gower's sign** is classical of **Duchenne's muscle dystrophy** but may be seen in Becker's and myotonic MD.
- Pt without calf m/s hypertrophy can be identified by +nce of volley sign visible behind shoulders (**Pradhan sign**)
- Dystrophin is altered in size in Becker's, mutated (deletion defect) and -nt in Duchenne's and DCM
- Creatinine kinase-MM is most sensitive and specific marker for MD.
- **Duchenne's MD** is m/c hereditary muscle dystrophy
- Cardiomyopathy is usually a/w **Duchenne's**, **Becker's**, **Limb girdle**, **Emry Dreifuss muscle dystrophies**.
- **SCA (Spino cerebellar ataxia)** with retinal involvement - **SCA-7** in which macular dysfunction are seen.

DUCHENNE M/S DYSTROPHY (DMD)

- M/c hereditary muscle dystrophy. XR disorder
- DMD is present at birth but the disorder usually manifests b/w 2-5 yrs of age. The boy falls frequently. There is difficulty in keeping pace with friends while playing.
- By the age 5, parents notice that child gets up from the floor using his hands (**Gower's maneuver**)
- By the age 6, Contractures of heel cords and iliotibial bands are obvious. Toe walking is a/w lordotic posture.
- B/w the age 8-10, walking may require use of braces.
- By the age 12, most patients are wheelchair dependent.

- By the age 16-18, serious pulmonary infections/ aspiration pneumonia can lead to death.
- **Lab/f**: Serum CPK levels are 20-100 folds elevated. Definitive d/g is established by dystrophin deficiency in a m/s biopsy. Peripheral blood WBCs analysis reveals mutation (most commonly a deletion defect) of the dystrophin gene located on Xp21.
- **Prenatal d/g**: C/b made by western blot analysis of m/s biopsy specimens.
- Intellectual impairment is common.
- Cardiomyopathy is seen in almost all patients.

Floppy infant

- Scarf sign positive (Ragged doll on ventral suspension)
- **Werdnig Hoffman d/s** (Spinal m/s atrophy type 1) is char/ by marked hypotonia, sluggish fetal movement, fasciculation of tongue, poor cry, absent DTR. Ocular m/s and sphinctors are spared
- Fasciculations are most characterstic of spinal muscle atrophy.

JUVENILE RHEUMATOID ARTHRITIS (JRA)

- M/c type of JRA seen in boys--- Pauci-articular type 2
- Serious eye complications are seen in ---Type-1 oligoarticular JRA. Chronic and potentially serious ant. uveitis (iridocyclitis) +nt in 20-40% of pt. which leads to progressive blindness. The group which is ANA +ve (here 90%) appears to be at highest risk.

JRA Types

	Polyarticular RF -ve	Polyarticular RF+ve (seropositive)	Pauci articular		Systemic onset (Still's ds.) Quotidian
			Type I	Type II	
Frequency	20-30%	5-10%	30-40% (m/c)	10-15%	10-20%
Sex predilection	90% in girls	80% in girls	80% girls	90% boys	60% boys
Age of onset	Childhood, insidious	Adolescents	1-2 year	late childhood	childhood
RF	-	+(100%)	+	-	-
ANA	+(in 25%)	+(75%)	+(90%)	-	-
HLA	-	DR-4	DR-5, 6, 8	B-27	DR-4, 5
Joints involved	≥ 5 Erosive arthritis of large joints (wrist, elbow, ankle)	≥ 5 Small joints of hand of feet	≤ 4 (knee, ankle, elbow)	≤ 4 similar to type I + Hip, axial skeleton	Multiple joints, fever, HSM, maculopapular rash, abd. pain
Sacroiliitis	-	Rare	-	-	-
Iridocyclitis/uveitis	Rare	-	30% (chronic → blindness)	10-20% (acute, do not progress)	-
Prognosis	Better	Poor	good but blindness in 10%	good, a/w spondylopathy	poor

- M/c type of JRA --- Pauci-articular type 1.
- JRA is more common in girls (exception : Type-2 pauciarticular & systemic onset JRA are more common in boys)
- T/t of JRA --- Aspirin/ NSAID like naproxen. Steroids are required in systemic onset JRA, organ dysfunction, progressive d/s. Topical steroids are indicated in iridocyclitis

MITOCHONDRIAL MYOPATHIES

- Exclusively inherited from mother. (Because sperms do not have mitochondria)
- Kerns Sayre syndrome, Chronic progressive ophthalmoplegia, **LHON, MERRF, MELAS**
- Kerns Sayre syndrome is c/by triad of progressive external ophthalmoplegia + pigmentary degeneration of retina + onset < 20 yr of age.

ENDOCRINOLOGY

CONGENITAL ADRENAL HYPERPLASIA (CAH)

- Also k/as Adrenogenital syndrome .
- More common in females.
- M/c cause of CAH is 21α hydroxylase deficiency. AR condition

Salt Losing form
causes hypotension, shock

21-OH deficiency
(M/c form 95%, AR)

(also 3β HSD deficiency
behaves in same fashion; but
is rare)
** Lipoid enzyme defi.
also has same features
but has opposite effect on
genitalia)

Salt Retaining form
(causes hypertension)

11- β (OH)
deficiency 17- α -OH
deficiency

Male	Female	Male	Female
Normal genitalia but Later Precocious Puberty	Ambiguous Genitalia (FSH)	Ambiguous Genitalia	Normal genitalia / Precocious Puberty
↑ 17-OH-P, ↑ K ⁺ , Met. acidosis		↑ DOCS	↑ DOCS ↓ 17-OH-P
Treat shock		Mineralo + gluco replacement	

(FSH = Female pseudo hermaphroditism)

- 3- β -HSD deficiency is very rare form. Mild form is a/w precocious puberty, hypospadias in male. Severe form is salt losing, a/w virilization +, \downarrow synthesis of all adrenal steroids. \uparrow 17 OH pregnanolone and DHEA

- 21-hydroxylase deficiency is the m/c cause of ambiguous genitalia in the newborn & m/c cause of CAH.
- 17-hydroxy progesterone (17-OH-P) in blood & urine is the most important screening test to diagnose and differentiate various forms of CAH
- Prenatal t/t of CAH is possible. At risk pregnant mothers are started with dexamethasone at 6 weeks of gestation f/b a CVS at 11-12 week to confirm sex of the fetus. Continue t/t only if the affected fetus is female. If fetus is male stop t/t.

Imp. causes of ambiguous genitalia

In boys (46 XY)

- Testosterone synthesis defect
- Leydig cell hypoplasia/ receptor defects
- Androgen insensitivity syndrome (AIS)
 - Complete AIS d/to receptor mutation
 - Partial AIS (Reifenstein syndrome)
 - 5 α reductase def. a/w perineo-scrotal hypospadias
- Gonadal dysgenesis
- Congenital anomalies of mullerian structures.

In girls (46 XX)

- CAH, adrenal/ gonadal tumours
- Maternal androgens
- Placental aromatase deficiency

Interpretation of thyroid function tests:

T ₄	FT ₄	TSH	Interpretation
\downarrow	\downarrow	\uparrow	Primary hypothyroidism
N	N	\uparrow	Transient compensated hypothyroidism
\downarrow	\downarrow	N	Central hypothyroidism
\uparrow	\uparrow	N	Hyperthyroxinemia
\downarrow	N	N	Low TBG
\uparrow	\uparrow	\uparrow	T ₄ Resistance

Hypothyroidism

- M/c preventable cause of mental retardation is congenital hypothyroidism..
- M/c cause of congenital hypothyroidism is thyroid dysgenesis (dyshormonogenesis).
- Screening tests : Cord blood FT₄ & TSH. TSH is single best indicator.

- Best time for test is : 2days - 6 days. In first 24 - 48 hrs : there is TSH surge. False +ve results are more with cord blood.

Neonatal Hypothyroidism

- M/c neonatal disorder to be screened in neonatal period.
- Blood sample is collected from cord's blood.
- Test involve FT₄ and TSH.

PRECOCIOUS PUBERTY (PP)

Type	Causes
Central isosexual PP	
Idiopathic	Sporadic, familial
Organic neurogenic	CNS tumours - craniopharyngioma CNS infections - TB, Post meningitis CNS insult - Trauma, neuro Sx, radiation Malformation- Arachnoid cyst, hydrocephalus

Variation in pubertal devt

Isolated cause	Isolated premature thelarche Isolated premature pubarche/ adrenarche Isolated premature menarche
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Peripheral PP in girls

Hypothyroidism	
Ovarian estrogen	McCune Albright syndrome, Benign follicular cyst, Granulosa theca cell tumours
Adrenal estrogen	Feminising adrenal neoplasia
Exogenous estrogens	Phytoestrogens, creams

Peripheral PP in boys

CAH	21-hydroxylase deficiency, 11 β -hydroxylase deficiency
Adrenal tumours	
Testicular tumours	Leydig cell, adrenal rest tumour
Testotoxicosis	
h-CG secreting tumours	
Exogenous	Androgen/testosterone exposure

Heterosexual PP

Virilisation in girls	CAH, PCOS, ovarian hyperplasia
Feminisation in boys	Estrogen producing adrenal tumour, Exogenous estrogen/drugs

KIDNEY AND GUT

- Complement C3 levels will be low in post infective GN, MCNS and SLE (lupus nephritis), but will be normal in IgA nephropathy and Good Pasture d/s
- Renal parenchymal d/s constitute 78% of all (of which chronic glomerulonephritis is the m/c cause) cases of hypertension in children.

Imp. causes of hematuria

Streptococcal/

Post-infective GN	---	C3 low
IgA nephropathy	---	C3 normal
RPGN	---	fatal progression
SLE	---	ANA, ds DNA +ve . C3 low
Nephritic onset		
nephrotic syndrome	---	Massive proteinuria, high s. cholesterol
Alport	---	familial, deafness, lens dislocation
HUS	---	Bleeding, hemolytic anemia, thrombocytopenia

UTI

- Chances for renal scarring are more in children below 4 years and those with anatomical defects esp in male
- Definitive d/g of UTI depends on the urine culture showing 10^5 or more bacteria/mL
- DMSA scan is used to confirm scarring of kidney. DTPA and MAG3 are used to assess functions of kidney.
- M/c cause of UTI in children → VUR.
- VCUg or MCU is indicated to delineate VUR.

Direct radionuclide cystography (DRCG) is indicated whenever detection of VUR is important. Main clinical indications are:

- A. Detection of VUR in children after UTI (in boys the first catheter cystogram should be an MCU to visualise the urethra).
- B. Follow up of children with known VUR during prophylactic antibiotic/bacteriostatic treatment
- C. Assessment of the results of endoscopic or surgical treatment.
- D. Screening of siblings of children/parents with proven VUR

DRC can be also used for the detection of VUR in renal transplant recipients and for serial evaluation of bladder dysfunction (e.g. neurogenic bladder) for reflux.

Contra indications

There are no contraindications. However children should not be catheterised during the active phase of UTI.

- M/c finding on VCUG, done for evaluation of UTI, is vesicoureteral reflex (VUR)
- Fever with chills, loin pain and plenty of pus cells with pus casts in urine indicates—pyelonephritis

CNS

Meningoencephalitis in Children

- M/c cause of meningoencephalitis in children is enteroviruses.
- M/c sporadic cause of encephalitis → HSV.
- HSV Encephalitis : Char/by temporal lobe involvement with focal/ complex partial seizures. HSV is the m/c cause of severe and sporadic encephalitis. In MRI on T2 weighted image and in FLAIR image high signal intensity lesions are seen in orbitofrontal, anterior and medial temporal lobes in most patients within 48 hour of onset of symptoms.
- Epidemics of encephalitis during summer month are produced by arboviruses (JE is most common).
- Encephalitis + 8th CN damage/ hearing loss ---- Mumps .
- Encephalitis following a live virus vaccination can occur after ---- Measles, Mumps, Rubella, Polio.

MENINGITIS IN CHILDREN

- Newborn : GBS are the m/c cause f/b gram negative bacilli.
- Infancy : H. influenzae type B is the m/c cause in India. Meningococcal in developed countries.
- Child with complement deficiency (C5-C8): Recurrent meningococcal meningitis.
- CSF leak, cochlear implants predispose the child for: Pneumococcal meningitis.
- CSF shunt infection predispose the child for : Coagulase negative staphylococci
- A child with Lumbosacral dermal sinus and meningocele : Staphylococci, Gram -ve enteric bacilli.
- A child with T-lymphocyte defect: Listeria monocytogenes.
- A child splenic dysfunction, SCD, asplenia is at risk of : Sepsis and meningitis with capsular organism (pneumococcal, Hib, meningococci)

Febrile Seizures Children

- M/c cause viral URI
- 6 month- 5 yr children are affected.
- Prophylaxis by clobazam (if available) 0.5-1 mg/kg/d for 48 hours. or by P/R diazepam.
- Antipyretics, tepid sponging & inj. Midaz/Lorazepam SOS.
- Usually single episode & prognosis is good. There is no residual neurological deficit.

Specific disorders of neuronal migration

- Lissencephaly.
- Pachygyria
- Polymicrogyria
- Focal cortical dysplasia
- Miller-Dieker syndrome
- Muscle brain eye syndrome
- Fukuyama congenital MD

POINT OF SPECIAL MENTION

- Hemophilus influenzae infection produces effusions in the vicinity of infection site.e.g.
M/c complication of H. influenzae meningitis in infants --- Subdural effusion
H. influenzae infection of ear in children leads to --- ASOM and glue ear (Otitis media with effusion)
H. influenzae infection of lower respiratory tract leads to --- Pneumonia with effusions
- A neonate with recurrent infections and abscess is diagnosed as Kostmann syndrome (severe congenital neutropenia)
What is the t/t --- G CSF
- There is no role of sodabcarb & aminophylline in neonatal resuscitation now a days.
- During labour suction of meconium with the delivery of head of the baby is NOT recommended now-a- days
- Childhood cholelithiasis is seen in → Neiman Pick d/s.
- DOC for Kawasaki d/s → Immunoglobulins.

SOME IMP. NEGATIVE POINT

- Steroids are NOT useful in --- MPGN
- Raised ICT in an infant is NOT diagnosed by --- Papilloedema
- NOT a cause of prolonged unconjugated jaundice in a newborn --- Septicemia
- Virilization of female is NOT seen in --- 17- α hydroxylase

def.

- NOT seen in cretinism --- Hypoglycemia
- Infantile body proportions are NOT seen in --- Malnutrition
- Cardiac defect NOT common in congenital Rubella --- ASD
- Incidence of HMD is NOT increased by --- IUGR, Chronic placental insufficiency, addiction (Narcotic) of mother
- Cerebellar atrophy or diffuse cortical atrophy is NOT seen in --- Congenital Toxoplasmosis
- Type of pulmonary stenosis NOT seen in TOF --- Supravalvular (infundibular, valvular & subvalvular may be present)
- In cold injury to preterm infant, what is NOT seen --- Shivering
- Erythroblastosis fetalis does NOT involves --- Anti-lewis blood group
- Five cleans of intranatal care does NOT includes --- Clean perineum
- NOT a complication of gestational DM --- Hydrocephalus
- Complication of severe malaria which is NOT common in children --- Deep jaundice, ARF, pulmonary edema
- NOT included in autistic disorder --- Visual impairment
- NOT indicated in a child with stridor and barking cough only --- Antibiotics
- NOT a factor contributing progression to epilepsy in a child with febrile seizure --- Age of presentation of febrile seizure
- NOT an impending sign of Eisenmenger complex --- Accentuation of tricuspid and pulmonary flow murmurs.
- NOT true of congenital toxoplasmosis complex --- Dye test is gold standard for Ig G..

CLINICAL VIGNETTES

- 1. A lady delivered a baby by NVD at 31 weeks of gestation. 6 hours later baby developed tachypnea and respiratory distress. CXR showing air bronchogram and ground glass appearance. Most likely diagnosis is [DNB HRH '08]
A. HMD
B. MAS
C. TTNB
D. Congenital Pneumonia
(Ans. A. HMD)
Respiratory distress and tachypnea is seen in all above 4 conditions. But

HMD is seen in preterm baby. Its onset is within 6 hours of birth. CXR shows air bronchogram + ground glass app
MAS is common in term/ post term baby, there is h/o intrauterine distress. CXR reveals coarse granular opacities

TTNB is common in term LSCS baby, Its onset is within 24 hours. CXR reveals prominent interlobar fissure

Cong pneumonia is suspected if there were any risk factors in mother like PROM, foul smelling liquor. CXR findings are s/o pneumonitis.

- ❑ A 10 month old baby, who was previously normal, developed sudden distress in his crib. The external appearance of genitalia was normal, except hyperpigmentation. Blood glucose level was found to be 30 mg%. What is the most likely diagnosis:- [AIIMS May'2009]

A. 21-hydroxylase deficiency
B. Hyperinsulinism
C. Familial glucocorticoid deficiency
D. Cushing's syndrome

(Ans. C. Familial glucocorticoid deficiency)

- ❑ A 1 year old boy is brought to you with complaints of developmental delay,, constipation and dry skin. On examination a goiter can be palpated. The most likely diagnosis is [AIPGMEE'2011]

A. Thyrotropin receptor defect
B. Dyshormonogenesis
C. Thyroid dysfunction
D. Central hypothyroidism

[Ans.: B. Dyshormonogenesis]

M/c cause of congenital hypothyroidism is abnormal development of gland i.e. dyshormonogenesis.

- ❑ A 10 yr old girl presents with the history of recent seizures. She is a known case of nephrotic syndrome and is on mutiple medications including tacrolimus. Her temperature is 97o F BP is 130/80 mmHg, pulse is 78/min and RR is 16/min. Lab parameters are Na⁺ 135, Urea 79, Cr 0.5, albumin 1.5, Total Ca⁺⁺ 7.5, albumin 2 gm%. Most likely cause of her seizures is : [AIPGMEE'2012]

A. Tacrolimus toxicity
B. Hypocalcemia
C. Hyponatremia
D. Uremia

(Ans.: A. Tacrolimus toxicity)

Serum Na⁺ is within normal range and urea /creatinine are not in range of ARF so option C,D are ruled out.

Serum calcium is low bur s. albumin is also low. As we know that with every 1 g ↓e in albumin (here ↓e of 2 gm) value serum Ca ↓es by 0.8, so the corrected calcium here is $2 \times 0.8 = 1.6 + 7.5 = 9.1$ mg% which is within normal range and unlikely to produce seizures.

Tacrolimus can cause seizures d/to neurotoxicity, which can occur in >50% of patients.

- ❑ A 5 year old boy is detected to be HbS Ag positive on two separate occasions during a screening program for hepatitis B. He is otherwise asymptomatic. Child was given 3 doses of recombinant HB vaccine at the age of 1 yr. His mother was treated for chronic hepatitis infection around the same time. The next step in further investigating this child is-

[DNB HRH '08, AIPGMEE 2003]

A. Obtain Hbe Ag and anti-Hbe levels
B. Repeat Hbs Ag
C. Obtain anti HBs Ab levels
D. Repeat another course of HB vaccine
(Ans. Obtain anti - HBs Ab levels)

Immune status of a previously vaccinated child is best revealed by obtaining anti HbS Ab levels.

- ❑ Ramu, a 8 year old boy presents with upper GI bleeding. O/E, he is found to have splenomegaly; there are no signs of ascites, or hepatomegaly; esophageal varics are seen on upper GI endoscopy. Most likely d/g is.

A. Budd chiari syndrome
B. NCPF
C. Cirrhosis of liver

D. Veno-occlusive d/s [AIPGMEE 2001]
(Ans. D. Veno-occlusive d/s)

Patient's profile and diagnostic Clue

Features	NCPF	EHPVO	Cirrhosis
1. Age group	3rd - 4rd decade	1st - 2nd decade	
2. Site of obstruction	major br of portal v. thrombosed	smaller br. of portal v.	
3. Splenomegaly	+	+	+
4. Hepatomegaly	-	-	-
5. Ascites	-	-	+
5. Variceal bleeding	+	+	+
6. Jaundice	-	-	+
7. hepatic vein wedge pressure	Normal / mildly raised	low	raised

Diagnostic triad in NCPF include patent splenoportovenal axis, absence of cirrhosis, and presence of portal venopathy

(here esophageal varices and UGI bleed) involving 3rd and 4th degree intrahepatic venules.

- A 10 year old boy presents with pain in right hypochondrium since 2 days. His Hb is 9.69%. His mother gives h/o passing black stools for 7 days and 2-3 occasions in the past 2 yrs. During these episodes he had fatigability while playing and was not able to play with his peers. Which of the following will maximally help to arrive at a clinical d/g

A. Pallor
B. Jaundice
C. Palpable spleen
D. Free fluid in the abdomen.

(Ans. C. Palpable spleen) [AIIMS'2010]

Pain in RUQ c/b due to splenic enlargement secondary to portal HTN. M/c cause of portal HTN in children is EHPO in children <10 yr. Black colored stools indicate malena, which further results in anemia (low Hb). Combination of upper GI bleed + splenomegaly is strongly s/o EHPO. Had it been similar presentation in older child, the diagnosis could be NCPF.

- A child presented with absent thumb, bowing of the forearm bones with thrombocytopenia. The investigation not useful in this condition [AIIMS'2008]

A. Karyotyping
B. Bone marrow examination
C. Echocardiography
D. Platelet count

(Ans: Echocardiography)

Child has features of Fanconi anemia, which require BME, platelets, karyotyping to diagnose the condition.

- A 5 year old child was brought with tall stature, behavioral problems and mental retardation. The child had an affected elder sibling with similar features and blindness. He also had a normal sibling. The child had tall stature, arm span more than height, elongated thumb, arachnodactyly, positive wrist sign and positive Steinberg sign. with adducted thumb reaching beyond the palm. The child is blue eyed blonde with malar flush. Examination of eyes revealed ectopia lentis, iridodonesis and cataract. Most likely diagnosis is:-

A. Phenylketonuria
B. Homocystinuria
C. Marfan syndrome

D. Alkaptonuria
(Ans. Homocystinuria)

Diagnostic clues.

All above mentioned features are characteristic of homocystinuria

Similar features but without mental retardation are seen in **Marfan's**

Blue eyed blonde + eczema + hyperactivity with positive urine FeCl_3 or Guthrie test in blood indicates **PKU**.

- A baby that was apparently alright at birth begins to show a delay in motor development by 3 months of age. At 1yr of age child begins to develop spasticity and writhing movements. At age 3, compulsive biting of fingers and lips and head banging appear. At puberty the child develop arthritis and died from renal failure at 25. The condition of this child was most likely due to deficiency of which enzyme

A. Hexosaminidase A
B. HGPTRase
C. Adenosine deaminase
D. Phosphorylase

(Ans. B. HGPTRase)

Child is suffering from **Lesch-Nyhan syndrome**, a rare inherited disorder caused by deficiency of HGPRTase, which causes accumulation of uric acid in all body fluids--- hyperuricemia and uricosuria. It manifests in first year as severe gout, renal problems, poor m/s control, and moderate mental retardation. In the 2nd yr of life self mutilating behaviour develops.

- A 10 month old baby, who was previously normal, developed sudden distress in his crib. The external appearance of genitalia was normal, except hyperpigmentation. Blood glucose level was found to be 30 mg%. What is the most likely diagnosis:- [AIIMS May'2009]

A. 21-hydroxylase deficiency
B. Hyperinsulinism
C. Familial glucocorticoid deficiency
D. Cushing's syndrome
(Ans. C. Familial glucocorticoid deficiency)

- A 2 month old child presented with failure to thrive, recurrent emesis, hepatosplenomegaly, and adrenal

calcification is noted radiologically. Most likely diagnosis is:- [AIIMS May'2009, May 2010]

- A. Adrenal hemorrhage
- B. Wolman's disease
- C. Pheochromocytoma
- D. Addison's disease

(Ans. B. Wolman's disease)

Wolman d/s is an AR condition caused by mutations in the gene encoding human lysosomal acid lipase. In this condition cholesterol esters accumulate in most organ systems leading to organ failure. Patient usually presents at 1-2 month of life. Death usually occurs in 1st year of life.

A 5 year old boy presents with pubic hair development. He is tall and has increased pigmentation of his genitalia and there is phallic enlargement. His BP is 130/90 mmHg. Measurement of which of the following hormone would be diagnostic? [AIPGMEE' 2009]

- A. 17- hydroxyprogesterone
- B. 11-Deoxycortisol
- C. Aldosterone
- D. Deoxycorticosterone

(Ans.: B. 11-Deoxycortisol)

Child is having precocious puberty, hyperpigmentation, hypertension. All these features are suggestive of adrenogenital syndrome. Prepubertal boys develop secondary sexual characteristics without the testicular growth, called precocious pseudo puberty. Two forms are seen --- first is salt losing form is common and second is hypertensive form (as in question) d/to excessive secretion of 11-DOC

A 5 year old girl presents with hypertension and virilization. Investigations reveal low Plasma Renin Activity and hypokalemia. What is the likely etiology? [AIIMS May'07]

- A. 21 hydroxylase deficiency
- B. 3 beta hydroxysteroid deficiency
- C. 11 beta hydroxylase deficiency
- D. Conn's disease

(Ans. : 11 beta hydroxylase deficiency)

Low plasma renin activity is seen in --- mineralocorticoid excess d/to defect in cortisol pathway e.g. 11 β hydroxylase deficiency and 17 α hydroxylase deficiency. Virilization +

hypertension + hypokalemia is seen in 11 β hydroxylase deficiency

Virilization + salt loss (hyponatremia, hyperkalemia) is seen in 21 hydroxylase deficiency

A 7 yr old child is brought to the OPD with complaints of ambiguous genitalia noticed since birth but becoming more readily noticeable with age. On examination child is of normal weight and height BP is normal but no generalised hyperpigmentation. Labial folds are bifid with two separate perineal openings and phallic length is 2.5cm with no meatus at the tip of phallus. Gonads are not palpable in inguinal region or in labial folds. Ultrasonography shows presence of Mullerian structures. What is the most likely diagnosis - [AIPGMEE'12]

- A. Simple virilizing congenital adrenal hypoplasia
- B. Complete androgen insensitising syndrome
- C. 5- α reductase deficiency
- D. Maternal virilizing tumour

[Ans. C. 5- α reductase deficiency]

Meatus is not at the tip of phallus means there is **hypospadias**. Hypospadias is a/w 5- α reductase deficiency.

5- α reductase deficiency is a/w \downarrow DHT production \rightarrow Severe ambiguity of external genitalia. Phenotypically they are boys with small phallus, bifid scrotum and perineal hypospadias.

A 4 week female infant presented to the emergency department with hyponatremia and hyperkalemia. Other than cardiovascular abnormality and dehydration, the physical examination findings are normal. The most informative laboratory examination would be [AIIMS May'2009]

- A. 17- (OH) progesterone
- B. Renin
- C. Aldosterone
- D. Cortisol

(Ans. A. 17- (OH) progesterone)

Clinical findings of hyponatremia, hyperkalemia and dehydration are consistent with congenital adrenal hyperplasia (CAH). **17- hydroxy ketosteroid** in blood/urine will help in differentiating the type of CAH. *Diagnostic clues.*

- 21-hydroxylase deficiency --- \uparrow 17-OH-P
- 11- β -hydroxylase deficiency --- \uparrow 11-DOCS
- 17- α -hydroxylase deficiency --- \uparrow DOCS + \downarrow 17-OH-P

A 7 year old child with a 3 year history of cough, intermittent wheezing, and poor growth has 2 sweat chloride value of

36 and 41 meq/L. Additional diagnostic testing to rule out cystic fibrosis should include

- A. CT chest
- B. Nasal pd-n measurment
- C. Fat balance (72 hour stool fat) measurement
- D. DNA analysis for F508 mutation

(Ans. B. Nasal pd-n measurment)

[AIPGMEE' 2009]

- A 8 year old boy presents with seizures. O/e his BP is 200/140 in upper limbs. His femoral pulses are not felt. Most likely d/g is :---

[AIPGMEE' 2010]

- A. Takayasu's aortoarteritis
- B. Renal parenchymal d/s
- C. Status epilepticus
- D. Grandmal seizures

(Ans. A. Takayasu's aortoarteritis)

Takayasu's aortoarteritis : HTN occurs in 32-925 of patients which contributes to renal, cardiac and cerebral injury. Cerebral injury in turn may precipitate seizures. Takayasu d/s should be suspected in any patient with absent or poor peripheral pulsations, discrepancies in BP, and arterial bruits.

- A 6 year old boy presents with Muscle weakness and positive Gower's sign. Lab/f reveals CPK value of 10,000 units/L. Most likely d/g is :---

[AIPGMEE' 2010]

- A. Duchenne's m/s dystrophy
- B. Becker's m/s dystrophy
- C. Congenital m/s dystrophy
- D. Myotonia congenita

(Ans. A. Duchenne's m/s dystrophy)

Duchenne's m/s dystrophy is also k/as pseudohypertrophic m/s dystrophy. Characteristically there is +ve Gower's sign and CPK values are highly elevated. See table in m/s disorder section for details.

- A 7½ old girl presents with a history of low-grade fever, non-productive cough, and mild dyspnea. After treatment with an oral antibiotic, the child began to show some signs of improvement. However, the child subsequently experienced increasing dyspnea, a productive cough, and wheezing. A chest radiograph demonstrates HYPERLUCENCY. Spirometry shows a severe obstructive pattern. The most likely diagnosis is:

[AIIMS May'07]

- A. Pulmonary alveolar microlithiasis.

B. Post viral syndrome.

C. Follicular bronchitis.

D. Bronchiolitis obliterans.

(Ans:- D. Bronchiolitis obliterans)

Cl/F are in favor of BO. Bronchiolitis obliterans is the only indication for use of steroids in an infant with bronchiolitis.

- 3.5 kg term male baby born of uncomplicated pregnancy developed respiratory distress at birth not responded to surfactant, ECHO is normal, CXR shows ground glass appearance. culture negative. apgar score 4 and 5 at 1 and 5 min. History of 1 month female sibling died before diagnosis?

[AIIMS Nov' 2008]

A. TAPVC

B. Meconium aspiration

C. Neonatal plmonary alveolar proteinosis

D. Diffuse herpes simplex infection

(Ans. C. Neonatal plmonary alveolar proteinosis)

Neonatal plmonary alveolar proteinosis is an AR condition.

	Age/etio	C/F	Inv
BO	Viral	Cough, fever, cyanosis, dyspnea, and RD	Normal or hyperlucency, patchy infiltrates
PAM	Familial, ?AR	DOE, non productive	b/L sandlike, micronodular opacities
NPAP	AR, Abnormal protein B,C, or GMCSF	All babies die	No t/t, lung transplantation is the only t/t.
Follicular bronchitis	Viral, 6-18 mo	cough, moderate RD fever, fine-crackles	Initially mild changes later interstitial pattern
IPH	<10 yr	Good Pasture syndrome pulmonary h'age wheezing, cough, dyspnea hyperaeration	Obstructive pattern PFT

D/d of Respiratory distress in newborn

Feature	RDS	MAS	Neonatal pulmonary alveolar proteinosis	TAPVC
Onset	within 6 hrs.	within 6 hrs	Immediately after birth	Immed. after birth
Risk-factor	preterm,* gestational DM	MSL, Listerosis, Post-term/term, Intrauterine asphyxia,	Familial, AR mother, foul smelling liquor Fetal distress	
CL/f	Cough, fever, cyanosis,	DOE, non productive	prgressive RD	Cyanosis and severe tachypnea at birth
CXR	b/B fine reticulonodular pattern, Air bronchogram	Coarse granular opacities, emphysematous / air trapping)	pneumonitis hyperinflated CXR	Figure of '8' or snowman sign
Physiology	Severe ↓ in compliance without any change in resistance	Markcdly ↑ resistance with some ↓ in compliance	Intraalveolar accumulation of surfactant lipoproteins	Severe obstruction to pulmonary venous return
Comment	Benefits from surfactant therapy		Pneumonitis	ECHO Large RV

Diagnostic clues are

- TAPVC ruled out as ECHO normal
- HMD ruled out as baby is term
- Cryptogenic organising pneumonia is synonymous with the bronchiolitis obliterans organising pneumonia.
- Idiopathic pulmonary fibrosis (cryptogenic fibrosing alveolitis) is also a related condition in which there is patchy fibrosis on X-ray. Fibroblast proliferation and fibroelastosis on biopsy is seen.

- As there is no cardiovascular /hemodynamic instability so the lesion is below medulla (option D ruled out)
- As there is RR is 30/min, diaphragmatic involvement is unlikely, phrenic nerve root i.e. C3-C5 should be unaffected. (option A ruled out)
- Quadriplegia denotes lesion above C5 (option C ruled out)

Hence C5-C6 is the level of lesion

A 7 year old girl with non productive cough, mild stridor for 3 months duration. Patient is improving but suddenly developed wheeze, productive cough, mild fever and hyperlucency on CXR and PFT shows obstructive curve. diagnosis is? [AIIMS Nov'08]

- A. Bronchiolitis obliterans (BO)
 - B. Idiopathic Pulmonary Hemosiderosis (IPH)
 - C. Pulmonary alveolar microlithiasis
 - D. Follicular bronchitis
- (Ans.- A. Bronchiolitis obliterans)

See above tables

A 8 year old boy presents with h/o fall followed by quadriplegia and urinary incontinence. O/e RR is 30/min, HR 110/min sensory level is at upper sternum. Level of lesion is. [AIPGMEE' 2010]

- A. C1-C2
 - B. C5-C6
 - C. T1-T2
 - D. Medulla.
- (Ans. B. C5-C6)

Child has presented with quadriplegia, bladder involvement and sensory level of upper sternum, no respiratory distress, no cardiac involvement.

A 8 year old girl presents with frequent staring looks lasting for 20 seconds. Episodes were observed by parents during the day time. On EEG 3Hz spike and wave pattern was seen. Most likely d/g is :--- [AIPGMEE' 2010]

- A. Day dreaming
 - B. Myoclonic seizures
 - C. Status epilepticus
 - D. Absence seizures
- (Ans. A. D. Absence seizures)

Absence seizures are c/by sudden, brief lasting for seconds lapses of consciousness without loss of postural control. On EEG characteristic 3Hz spike and wave pattern is seen.

A 2 year old boy presents with seizures. O/e hypopigmented patch was found over lumbosacral area. Most likely diagnosis is :--- [AIPGMEE' 2010]

- A. Tuberous sclerosis
 - B. Neurofibromatosis
 - C. Sturge Weber syndrome
 - D. VHL syndrome
- (Ans. A. Tuberous sclerosis)

Child presents with neurocutaneous disorder (Sx + skin

lesion). Major neurocutaneous syndromes include :

1. Tuberous sclerosis
2. NF
3. VHL syndrome

Tuberous sclerosis is c/by mental retardation, seizures + cutaneous manifestations in the form of hypopigmented macules/ patches (ash -leaf spots), adenoma sebaceum.

Sturge Weber syndrome is c/by hemiatrophy of cortex, intracranial snail track calcification, seizures, glaucoma + cutaneous manifestations in the form of port wine stain.

Neurofibromatosis presents with multiple neuromas, hyperpigmentation, axillary freckles.

- Q A 7 yr old boy is operated for craniopharyngioma. He develops deficiency of multiple pituitary hormones. Which of the following hormone should be replaced first.

[AIIPGMEE'2011]

- A. Hydrocortisone
- B. Thyroxine
- C. GH
- D. Prolactin

[Ans. C. GH]

At least two anterior pituitary hormones should be replaced after surgery for craniopharyngioma.

- Q Most important prognostic factor in congenital diaphragmatic hernia

[AIIPGMEE'2011]

- A. Degree of pulmonary hypertension
- B. Gestational age of neonate
- C. Size of hernia
- D. Age at the time of surgery

[Ans.: A. Degree of pulmonary hypertension]

- Q A term neonate 38 weeks / 2.2 kg develops feed intolerance on day2 of life. The sepsis screen is negative and there is no suggestion of intestinal obstruction. The PCV is 72% . What would the most appropriate action in this child?

- A. Keep the child NPO
- B. Medical management of intestinal obstruction
- C. Surgical management
- D. Partial exchange transfusion

(Ans. D. Partial exchange transfusion)

Polycythemia is a/w feed intolerance, so partial exchange transfusion c/b beneficial.

- Q A 30 weeks gestation mother delivered 1.2 kg baby with moderate respiratory distress. Vitals are RR = 70/min with grunting and chest retractions. What would the most

appropriate next action in this child?

[AIIMS Nov' 2010]

- A. Warm humidified O₂ via hood
- B. Nasal CPAP
- C. Surfactant and mechanical ventilation
- D. Mechanical ventilation only

(Ans. B. Nasal CPAP)

CPAP helps mainly by preventing the alveolar collapse in infants with surfactant deficiency. Once atelectasis and collapse have developed, CPAP might NOT help much. Therefore all preterm babies <35 weeks with any sign of respiratory distress should be started on CPAP.

CPAP is the established first line t/t in the m/m of respiratory distress in preterm VLBV infants.

Indications of CPAP are:

1. RDS
 - Mild RDS
 - FiO₂ requirement <0.4
 - PaCO₂ <55 - 66 mmHg
2. Apnea of prematurity
3. Post extubation in VLBW infants
4. TTNB delayed adaptation

Indications of surfactant are:

1. Rescue t/t in preterm infants with RDS
2. All preterm neonates <29 weeks of gestation.

- Q Ponderal index of a baby with weight of 200 gm and height of

[AIIMS Nov.' 2010]

- A. 1.6
- B. 2.2
- C. 2.6
- D. 3.6

(Ans.: A. 1.6)

$$\begin{aligned}\text{Ponderal index} &= \text{weight in kg} / \text{height (m)}^3 \\ &= 2 / 0.05 \text{ (m)}^3 \\ &= 1.6\end{aligned}$$

PI of <2 is seen in asymmetrical IUGR and PI of ≥2 in symmetrical IUGR.

- Q A 32 week newborn baby with RR 86/min and grunting presents with no nasal flaring, abdomen behind in movement than chest and no xiphisternal retraction. What is the Silverman score?

[AIIMS Nov.' 2010]

- A. 1
- B. 4
- C. 6
- D. 8

(Ans.: B. 4)

Silverman Anderson Retraction score

Score	0	1	2
1. Upper chest retractions	Synchronized	Lag on inspiration	See-saw movt.
2. Lower chest retractions	None	Just visible	Marked
3. Xiphoid retractions	None	Just visible	Marked
4. Nasal flaring	None	Minimal	Marked
5. Grunting	None	Stethoscope	Naked eye

So in the above question there is RR 86/min (no consideration in score) grunting presents (score 2) with no nasal flaring, abdomen behind in movement than chest means lower chest retractions are visible (score 1), minimal intercostal retractions (score 0) and no nasal flaring (score 0) no xiphisternal retractions (score 0).

Downes' score

Score	0	1	2
1. RR	<60	60-80	>80
2. Cyanosis	Nil	In room air	in $\geq 40\%$
3. Air entry	Normal	Mild	Marked
4. Retraction	None	Mild	Moderate
5. Grunting	None	Stethoscope	Audible/ Naked eye

The best possible score in each category is 0 and worst score is 2.s

- A 3 days old newborn baby vomits after each and every feeds, he has a distended abdomen and diarrhoea. The urine is positive for benedict's test for reducing substance. The substance in urine is ?

[AIIMS Nov.' 2010]

- A. Sucrose
- B. Glucose
- C. Galactose
- D. Fructose

(Ans.: C. Galactose)

Benedict test in urine c/b positive if any of the reducing substance is present in urine.

Vomiting after each and every feed/ feed intolerance, protruded abdomen are s/o galactosemia.

- A 15 days old breastfed term newborn develops seizures.

On investigations he is found to have S. cal of 5.4 mg% and serum phosphate of 9.8 mg/dL. His serum intact parathormone level was 30 pg/mL (normal range 10-65 pg/mL). The likely diagnosis is [AIPGMEE'2011]

- A. Vitamin D deficiency
 - B. Hypoparathyroidism
 - C. Pseudohypoparathyroidism
 - D. Hypoxic ischemic encephalitis
- (Ans.A. Vitamin D deficiency)

- An 8 yr old child presents with BP of 180/100 mm Hg, urea of 90, creatinine of 5.3, urine analysis shows 15-20 pus cells, 1-2 RBCs, protein 1+, and has no significant similar past history. The likely diagnosis is [AIIMS Nov '10]

- A. Post infective GN
 - B. Accelerated HTN with ARF
 - C. Idiopathic RPGN
 - D. Chronic interstitial nephritis with VUR
- (Ans. B. Accelerated HTN with ARF)

- A 6 week old male child presents to the casualty with failure to thrive, dehydration and shock. On examination he has generalized increased in pigmentation and normal male genitalia. His S. sodium is 128, K^+ is 6.5 and blood sugar is 30 mg%. The likely diagnosis is [AIPGMEE'2011]

- A. Congenital adrenal hyperplasia
- B. Sepsis with adrenal hemorrhage
- C. Acute gastroenteritis with dehydration
- D. Faulty feeding with diluted formula.

- A 2 yr old child completed 8 days course of cefaclor, presents with low grade fever, malaise, and irritability. On examination there is lymphadenopathy and generalized erythematous rash that is mildly pruritic. The most likely diagnosis is: [AIPGMEE'2011]

- A. Kawasaki disease
 - B. Partially treated meningitis
 - C. Infectious mononucleosis
 - D. Type III hypersensitivity reaction.
- (Ans.C. Infectious mononucleosis)

- A pregnant woman delivers a baby with birth weight 1500 gram and gestation 33 weeks. One examination vital parameters are normal. What would be the initial method of choice for feeding: [AIPGMEE'2011]

- A. Keep NPO and start IV fluids
- B. Start on oral feeding by intragastric tube alternate method
- D. Start IV fluids and oral feeds both

D. Start TPN

(Ans.: B. Start on oral feeding by intragastric tube alternate method)

NOTES

Initial feeding method in LBW babies

Gestation	Maturation of feeding skills	Initial feeding methods
<28	No proper sucking efforts, No propulsive motility in the gut	IVF
28-31	Sucking bursts develop, uncoordinated	OGT or SF with occasional SF/PF
32-34	Co-ordinated sucking and swallowing	SF
>34	Mature sucking pattern	BF

A large for date 4 kg baby is lethargic on clinical examination. The blood sugar on screening is 31 mg%. The next step is- [AIPGMEE'12]

- A. Give 1 Full measured EBM feed and then recheck sugar at 1 h.
 - B. Start I/V 10% Dextrose
 - C. I/V 10 % Dextrose bolus 2 mL/kg
 - D. Monitor RBS only
- [Ans. C. I/V 10 % Dextrose bolus 2 mL/kg]

We have to follow AIIMS protocol for hypoglycemia.

Algorithm for management of neonatal hypoglycemia

1. Blood sugar 20-40 mg/dL
 Trial of oral / fortified feeds (5g/100mL of sugar)
 Monitor the blood sugar after 1 hour
 and if it is > 40 mg/dL → Frequent feeds
2. Blood sugar <20 mg/dL in asymptomatic baby or any level <40 but symptomatic including seizures →
 Give a bolus of 2 mL/kg 10% and start
 IV glucose infusion @ 6 mg/kg/min
 Monitor hourly till euglycemic and then 6 hrly

PRINCIPLES OF RADIOLOGICAL PROCEDURES

Investigation Procedures in Radiology

Radiation producing modalities		Modalities which do not produce radiation
Ionizing	Non-ionizing	
1. CT	1. UV radiation	1. USG
2. X-ray (radiography)	2. Infrared radiation (Thermography)	2. MRI
3. γ -ray	3. Radiofrequency ablation	
4. α -ray	4. Microwave radiation	
5. β -ray (electrons)	5. Phototherapy for jaundice (visible light)	
6. Protons		
7. Fluoroscopy, DSA		
8. SPECT, PET		
9. Nuclear scans		

→ **SPECT** (Single photon emission computed tomography), **PET** & **MR spectroscopy** are some examples of functional imaging techniques.

→ **MRI** uses magnetic field to construct images.

→ **CT** uses radiation for constructing images.

→ **Ultrasound** is not mutagenic.

→ A pregnant lady should not be exposed to radiation producing modalities (esp Ionizing). Period when fetus is most sensitive to radiation is 8-15 weeks of gestation.

CONTRAST MEDIA IN RADIOLOGY

- Contrast agents are used for better visualization.
- Used in X-ray, fluoroscopy, Ba studies, CECT (contrast enhanced CT scan), angiography, arteriography etc.
- Barium & iodine compounds are most commonly used.
- 2 types:
 1. Ionic
 2. Non-ionic

Ionic - water solubles iodide dyes (e.g. Na- diatrizoate, meglumine, conray, urografin, angiografin) - may cause anaphylaxis, obsolete now a days

Non ionic - Safer but expensive e.g. iohexol (Omnipaque), Iopamiro.

Type	Subtype	Example
• Ionic	Monomer (HOCM)	Diatrizoate, conray
• Non-ionic	Monomer (HOCM)	Iohexal 300, 240 (Omnipaque)
	Dimer (IOCM)	Iodixanol (Visipaque)

- IOCM (Iso-osmolar contrast media) are most recent agents iohexanal 320 (Visipaque).
- Acute renal failure is m/c renal toxicity of contrast agents. Serum urea & creatinine values should be available before giving i/v contrast.

Contrast Agents used in various radiological procedures

Procedure	Contrast agent
• Cerebral angiography, Aortography	Conray 280
• Coronary angiography, CT-scan	Conray 420
• Hysterosalpingography	Conray 280/420
• DSA, Myelography, Ventricleulography	Iopamidol, Iohexol(omnipaque), Myodil, Metrizamide
• Bronchography, esophagoscopy (Esophageal atresia)	Dionosil (Tantalum)
• Oral cholecystography (OCG)	Ipanoic acid (Telepaque)
• IV cholecystography	Biligriffin
• Patency of recut Sx anastomosis (Idiopathic megacolon/Hirschprung's d/s)	Gastrografin enema
• MRI	Gadolinium
• IVP	Na- diatrizoate, hypaque

ULTRASOUND (USG)

- Based on **piezoelectric** effect of crystals made up of lead zirconate titanate.
- No radiation exposure
- Pizoelectric effect**: Ability of some material to change their physical dimensions when an electric voltage is applied. Converts electric voltage to sound energy and vice versa.
- In medical ultrasound frequencies commonly used are 2-10 MHz (>20,000 KHz).

- Father of obstetric ultrasound - Ian Donald.
- Investigation of choice for obstetric conditions.
- Useful in differentiating solid and cystic lesions. **Sensitive in diagnosing acute appendicitis, blunt abdominal trauma & gall stones** (but less sensitive for UC, ureteric calculi, pancreatic ds)
- *Frequencies used in various USG probes*

Type of ultrasound	USG frequency
◦ Trans abdominal	3-5 MHz
◦ Trans vaginal	5-7.5 MHz
◦ USG for breast	15 MHz
◦ Endoscopic USG for gut wall	7.5-20 MHz
◦ To image vessel wall via catheter	20 MHz

- *3 types of image display*
A - mode --- used only in eye scan
B - mode --- M/c in use
M - mode --- used in moving part like vulvular heart d/s (e.g. in ECHO)

- *USG findings & cause*

USG finding	Cause	Interpretation
◦ Acoustic shadows	Reflection	Stones (60% reflection), Tissue gas interface (100% reflection, so more dense shadows)
	Absorption/attenuation	Fibrous tissue, Fat (fatty liver)
◦ Edge shadows	Refraction	Cysts, fetal skull Neck of GB, Cooper's ligament of breast
◦ ↑ed through transmission	Opposite to attenuation shadow	Hallmark of cystic space

- *Hyperechoic and hypoechoic shadows on USG*

Hypo echoic	Hyperechoic/Echogenic
Metastasis to liver from ca ovary, bladder, stomach (mucinous adenocarcinoma)	Colon mucinous adenocarcinoma secondaries to liver, Hepatoma, treated breast cancer Adenomyomatosis

- USG causes delirious effect on small micro-organisms by acoustic cavitation.

DOPPLER

- Based on Doppler effect (change in the perceived frequency of sound emitted by a moving source measures blood flow). It provides both audio and video signals.
- **Types**
 - Continuous waves
 - Pulsed waves
- In Doppler imaging **colour** displays direction of blood flow. It is
Red --- when direction of flow is towards the transducer.
Blue --- if flow is away from transducer. (*Mnemonic: BART*)
Intensity of colour represents velocity of blood flow. lighter shades represent higher velocity
- *Used for*
Arterial stenosis (e.g. RAS, TAP, AV fistulas), carotid occlusion, PVD, Burger's disease.
DVT, varicose veins to find perforator incompetence

X-RAYS

- X- rays are produced when fast moving stream of electrons produced by cathode (tungsten filament) strikes the anode made of tungsten (**thermionic emission**).
- X-rays are short electromagnetic radiations produced by energy conversion when fast-moving electrons from the filament of the X-ray tube interact with the tungsten anode (target).
- Linear accelerator (Linac) and betatron are used to produce X-ray by accelerating electrons.
- They have higher frequency, greater power of penetration, high energy than particles.
- X- rays are most scattered by H^+ ion.
- *X- ray films:*
 1. Expiratory (& erect) film is required in pneumothorax & FB
 2. Inspiratory film is required for PA view CXR
 3. Barium-meal for hiatal disorders is done in Trendelenburg's position

→ Renal scan is done in prone position.

→ Aortic window is seen in LAO (Left anterior oblique) view.

- In radiographic imaging :
Contrast is ↑ by --- ↑ in current (mA)
Penetration is ↑ by --- ↑ in voltage (kVp)

Views of CXR to visualise various structures

View	For /Structure visualised
◦ Ipsilateral lateral decubitus	Minimal pleural effusion (<25 mL)
◦ Rt. anterior oblique	Rt lung, Lt. atrium enlargement, GB, mitral valve
◦ Lt. anterior oblique	Tracheal bifurcation, aortic window
◦ Rt. posterior oblique	Right retrocardiac space
◦ Rt. decubitus	Rt middle lobe, Rt. pleural effusion
◦ Lordotic view	Apex, lingual lobe (RML)
◦ Reverse lordotic view	Interlobar effusion
◦ Lateral skull view	Sella tursica
◦ Odontoid	C1 C2, (# of axis /atlas)
◦ Oblique	Spondylolisthesis, #scaphoid
◦ Skyline	Patella
◦ Stryker's	Recurrent subluxation / dislocation of shoulder
◦ Erect view	Pneumoperitonium

- "Golden-S sign" is seen in Rt upper lobe collapse
- In Chest X-ray PA view
 - Right heart border is formed by :
RA+ Innominate (right brachiocephalic) vein + SVC ± IVC (NOT formed by RV, ascending aorta)
 - Left heart border is formed by :
Aortic knuckle /arch + pulmonary trunk + LA

Views of X-ray for study of PNS / Orbit

View	Best to visualise	Also useful for	NOT useful for
1. Water's /OM	Maxillary sinus/ antrum (best)	Floor of orbit	Frontal sinus
2. Caldwell's/ OF	Frontal sinuses, SOF	Ethmoidal sinus	Maxillary antra
3. Lateral view	Sphenoid sinus		
4. Oblique	Ethmoidal sinus, optic foramen		
5. Stenver's/ Towne's	Mastoid air cells, petrous cells, internal acoustic meatus		

CT-scan or CAT scan

- Invented by Godfrey Hounsfield in 1963
- **Electron density** of tissues is numbered as **Hounsfield units (HU)** or **CT number**. Depends on linear attenuation co-efficient of the matter.
Density and Hounsfield units as noted on CT

Substance	Colour in CT	HU (CT units)
◦ Bone	Most white	750-1000
◦ Contrast	White	75-300
◦ Soft tissue	Grey	40-60
◦ Water	Dark grey-black	-10 to +10
◦ Fat	Black	-100
◦ Air	Most black	-500

◦ CT dose index (CTDI)

Becoz ionising radiation causes more biological effect in children, it is important to adopt CT technical parameters to minimize radiation dose. CTDI is m/c parameter to estimate & minimize patient dose in CT.

◦ Factors which influence radiation dose

1. K Vp (Kilo voltage) : Linear relationship with the radiation dose. ↑ in 120-130 kvp can double the radiation dose
2. Tube current (mA) : Linear relationship with the radiation dose. ↑ in mA by 50% can increase radiation twi
3. Pitch (thickness/ table speed) : Inverse relationship with the radiation dose.

◦ Two type of contrast agents are used

Ionic - water solubles iodide dyes (e.g. Na- diatrizoate, meglumine, conray, urograffin, angiografin) - may cause anaphylaxis, obsolete now a days

Non ionic - Safer but expensive e.g. iohexol (Omnipaque), Iopamiro

◦ Investigation of choice in imaging pancreas, adrenals, mediastinal mass. CT is superior to MRI for detection of calcified lesions of brain.

- Used for detecting asymptomatic atherosclerotic plaque by detecting the calcium deposition in the plaque, scoring system k/as **Agatston scoring**.

FLUOROSCOPY

- Study of moving body structures via X-ray.
- Sine radiography / fluoroscopy method is used for studying cusp movement of calcified aortic and mitral valves. In cineangiography **aortic valves are seen to move upwards** from the diastolic position like a piston to form a dome-

shaped structure.

- Used for transapical aortic valve implantation also.

MRI

- No radiation exposure becoz it is based on **gyromagnetic property** of protons (or H^+ ions / nucleus)
- It can be plain MRI or contrast MRI. M/c contrast agents used is i.v. Gadolinium DTPA.
- Proton density and relaxation time are assessed by radiofrequency pulse and the computer generates a gray scale image from this data.
- Magnetic field strength used for clinical imaging ranges from 0.02 to 8 Tesla.
- Relaxation time :**

T_1 : Time taken to return to original axis (T_1 images are used to find out normal anatomical details)

It has got high soft tissue discrimination (CSF looks black)

T_2 : Time taken by proton to displace. used to assess pathological processes (fluid looks white)

FLAIR image is Fluid attenuated inversion recovery image

- Characteristics of MR signals

Appearance of	T_1	T_2
	Spin lattice	Spin Spin
Water, CSF	Dark (hypo intense)	White
Fat	White	White
Subacute h/age, Posterior pituitary	White	
Ligaments/tendons, Cortical bone, Flowing blood	Black	Black

- C/I** - Patients with **prosthesis/implants** in the body, metallic foreign bodies, cardiac pacemaker, cochlear implants, cranial aneurysm clips, Swan Ganz catheter, bone growth/spinal cord stimulators, electronic infusion devices should never undergo MRI.
- Fear of spaces/ claustrophobia is common with MRI
- Since in MRI there are no beam hardening artefacts (as in CT), there is **superior imaging of the middle cranial fossa, skull base, neural canals, intraspinal contents, and bone marrow lesions.**
- MRI has high soft tissue contrast resolution with exquisite display of gray & white matter. *It is highly sensitive to presence of cerebral edema and for evaluation of chronic hemorrhages.*

- Epidermoids can be differentiated from arachnoid cysts on MRI by restricted diffusion.
- Cavernous angiomas on MRI are c/by smoothly circumscribed, reticulated popcorn configuration.
- MRI is inferior to CT for detecting calcification and/ or hyperostosis a/w brain tumors (e.g. meningioma).* It is also not as sensitive to acute hemorrhages as CT.
- MRI for tumours in relation to cavernous sinus:*
 - Meningioma : Isointense on T_1 & T_2 .
 - Cavernous hemangioma : Homogenous enhancement.
 - Schwannoma : Heterogenous.
- Farrady cage* is an electrical apparatus designed to prevent the passage of electromagnetic waves either containing them in or excluding them from its interior space.
- Mu copper foils* are applied for electromagnetic shielding of rooms.

PET

- Positron emitting radio nuclides are used:- O_2 informs oxygen uptake, CO_2 - informs CBF (cerebral blood flow), **18 FDG** - informs glucose utilization and is most frequently used moiety.
- Most frequently used moiety in PET is 2- $[^{18}F]$ fluoro-2-deoxy-D-glucose
- Indications**
 - To distinguish *radiation necrosis* from recurrent glioblastoma, viable from non-viable tissue in stroke
 - To evaluate degeneraⁿ, viability and monitor t/t response of brain tumor, recurrence potential of meningioma
 - To differentiate benign from malignant pulmonary nodules
 - For the d/g, staging, re-staging of colorectal, esophageal, head and neck, breast, lung cancers and lymphoma and melanoma.
 - For restaging of recurrent or residual thyroid cancers, of follicular cell origin.

DEXA

- Gold standard investigation for assessing bone mineral density..
- Particularly useful in post menopausal women.

SOME RADIOLOGICAL PROCEDURES

Obsolete Procedures/ Rarely used now a days

- Thermography** is based on IR rays. Reflects blood supply. Was used for breast tumour, carotid insufficiency, placental localization
- Myelography** is visualization of spine using non-ionic

water soluble dyes e.g. Iohexol, Omnipaque, Metrizamide, Iodixanol. Myodil was used in past which was oil based and was known to cause *arachnoiditis* (most serious c/c))

- Esophagoscopy/graphy, Bronchography: dye used was Dionosil

Lymphangiography

- Dye used is methylene blue/ lipoidal ultra fluid
- X-ray appearance
 1. Foamy/soap bubble appearance ---- Hodgkin's d/s
 2. Irregular filling defect ---- Sec./metastatic LN-path
 3. Marginal/ sun burst app ---- Reticulum cell sarcoma
 4. Coarse nodular storage pattern ---- Lymphosarcoma

Angiography

- In coronary angiography dye is injected through --- Femoral a.
- In cerebral angiography dye is injected through --- Femoral a.
- In fluoroscein angiography dye is injected through --- cubital vein

Oral cholecystography (OCG)

- Also k/as Graham Cole test, done to assess GB functions. It is Gold standard for demonstrating gall stones.
- Dye used is ipanoic acid (ipodate)

IV cholecystography

- Dye used - Biligrafin. GB is visualized in 15 min.

INTERVENTIONAL RADIOLOGY

- Involves procedures in which precision & radiological expertisation is required.
- Examples:
 1. *Percutaneous catheterization & embolisation*: Used in treatment of tumours. Embolisation ↓es vascularity & size of the tumour.
 2. *Percutaneous transluminal dilatation of stenosis*: Used in treatment of localized arterial stenosis.
 3. *Imaging guided needle biopsy*: USG/CT guided needle biopsy for lung/abdominal masses/tumours.
 4. *Needle puncture & drainage of cyst*: USG guided renal/ ovarian cysts.
 5. *Transhepatic catheterization of bile ducts*: For draining in obstructive jaundice/cholestasis.

RADIONUCLIDES

Radionuclides in imaging

Radionuclide	Procedure	Used for
Tc 99m labelled serum albumin		Pulmonary embolism
Tc 99m labelled RBCs		Imaging spleen, GI bleeding, ventriculography
Tc 99m DMSA	Static renal scintigraphy	For renal scarring, taken up by renal cortical cells
Tc 99m DTPA	Diuresis renography	Measures GFR, Renal tract obstruction
Tc 99m MAG3	Indirect MCU	VUR, transplant rejection
I-123 MIBG, I-123 Iodocholesterol,	Adrenal study	Adrenal medullary tumour
Tc 99m labelled HIDA		Heapatobiliary tree
Ga-67 nitrate		To detect tumours, concentrated in abscess cavity, inflammation

→ Tc 99m (99 is mass and m is metastable) is m/c used. It is administered IV and is pure γ rays emitter. Half life is short.

- Gadolinium** -- Paramagnetic contrast dye used in NMR (MRI)
- Xenon** -- For regional cerebral blood flow (CBF) studies
- Iodine-123** -- Evaluation of radio active Iodine uptake (RAIU)
- Iodine-131** -- For detection of thyroid cancer
- Cr⁵²** -- For Red cell survival studies.

INVESTIGATION OF CHOICE (IOC)

- Cardiotoxicity d/to radiotherapy/ chemo--- Endomyocardial biopsy
- Renal tuberculosis early stage-- IVP
late stage -- CT > IVP
- Acute aortic dissection -- TEE
- Avascular necrosis -- MRI
- Atypical cavernous hemangioma (mixed echogenicity) -- MRI
- Evaluation of breast implant -- MRI

- Chronic SAH -- MRI
- Acute SAH -- Non contrast CT head
- To localize site of bleed -- 4 Vessel X-ray angio
- Discrete swelling of thyroid (Solitary nodule) -- FNAC
- To localize site of bleed in SAH -- 4 Vessel X-ray angio
- EHBA -- Preop.cholangiogram
- For staging pelvic malignancy-- MRI
- Posterior fossa tumour -- MRI
- Meningeal carcinomatosis -- Gd enhanced MRI (contrast MRI)
- Acaustic/ vestibular neuroma -- MRI (Gd DTPA Enhanced)
- Parameningeal rhabdomyosarcoma -- MRI
- Nasopharyngeal angiofibroma-- CECT Scan
- Bronchiectasis -- HRCT
- ILD -- HRCT
- Pulmonary embolism -- CT chest with contrast
- Solitary pulmonary nodule -- CT
(CT helps differentiating malignant from benign by detecting calcification in benign)
- Blunt abdominal trauma -- CT Scan
- Osteoporosis -- DEXA scan
- For localizing epileptogenic foci
 - a. Structural imaging -- MRI, CT
 - b. Functional imaging --
(done only when structural imaging fails) -- PET, SPECT
- Stroke, hemorrhagic IOC -- NCCT
- Stroke, ischemic IOC -- MRI
- Aortic aneurysm, IOC -- CT scan
- Best evaluated by -- Angio/aortography
- Aortic dissection, IOC -- MRI
- If patient is hemodynamically unstable/ acute stage -- TEE
- Intraoperative monitoring -- TEE
- Gold standard -- CT (Aortography in the past)
- Cardiac tamponade, pericardial effusion -- 2-D ECHO
- DVT -- Venous USG
- Cardiac valvular disease -- M-Mode ECHO
- Anterior urethra is best visualized by -- Retrograde CUG

- Posterior urethra best visualized by -- MCU (Voiding cystogram)
- For entire urinary tract in emergency -- Non contrast spiral CT (Helical CT)
- Acute ureteric colic -- NC spiral CT abdomen
- Seminal vesicle, ejacul. duct-- Vasography
- Pheochromocytoma -- T₂ weighted MRI > CT
- Extra adrenal pheochromocytoma -- ¹³¹I-MIBG Scan
- Parathyroid adenoma -- Tc - Th subtraction scan
- Neuroendocrinal tumours (NENT) -- SRS
- Except insulinoma for which IOC is -- Endoscopic USG

Investigation of Choice

CT Scan (best for)	MRI	USG
• Bronchiectasis	• For pituitary & hypothalamic & optic chiasma lesion	• Pregnancy mass
• Pancreas	• cavernous sinus invasion	
• Adrenal	• Brain abscess	• Gall stones
• Acute SAH	• For spinal lesions except vascular malformation of spine (for which myelography)	
	• Prolapse IVD	
	• ICSOL (esp. post. fossa mass lesions)	

- *USG Abdomen* : to detect minimal ascites.
- *Echo*: is investigation of choice to detect minimal pericardial effusion, MS.
- *CT Abdomen & erect chset X-ray* : best to detect minimal pneumoperitoneum.
- *Angiography*: is investigation of choice for sequestration lung
- *MCU (Voiding cystourethrogram)*
 - For *posterior* urethra, PUV(posterior urethral valve), bladder neck (usually obstruction) in male.
 - To study bladder mechanism in stress incontinence
 - Recurrent UTI (but *not* for renal mass)
- *RUG*: Preferred for *anterior* urethra (but not done for posterior urethra)
- *Rapid sequence urography/pyelography* - for reno vascular hypertension
- *Bead Cystogram for* : Stress Incontinence
- *MRI for* :
Most sensitive modality for d/g of DCIS (Ductal carcinoma in situ)

SKULL , HEAD / BRAIN

Important findings of Skull

Findings	Condition
Geographical skull (lytic lesions+ bevelled edges)	Eosinophilic granuloma (Langhan's cell histiocytosis/ Hand-Schuller Christian d/s)
Multiple punched out lesions	Multiple myeloma
Brush border skull (Tru cut appearance)	Congenital hemolytic anemia/ Thalassemia
Hair on end appearance	Sickle cell anemia/ Thalassemia
Sutural diastasis	Raised ICT in children
Erosion of dorsum sella, Silver beaten appearance of vault	Raised ICT
Salt peeper skull	Hyperparathyroidism
Hot cross bun skull	Congenital syphilis

Sturge Weber Syndrome

- Neuroectodermal dysplasia
- Progressive hemiparesis, hemianopsia, mental retardation.
- Port wine stain (d/to cutaneous angiomas)
- Angiomas (hepato-meningeal angiomas with primary parieto-occipital distribution)
- Tram- line calcification (parieto-occipital)

Neuro-ectodermal dysplasia

- Neuro-fibromatosis
- Sturge Weber's
- Tuberous sclerosis
- VHL syndrome

Signs of raised ICT

In infants and children :

- Separation of sutures (Sutural diastasis is earliest change)
- Unusually thin skull vaults
- Presence of craniolacuniae
- The beaten-silver appearance. This is normal between 4-10 years.

In adults:

- Erosion of dorsum sellae is earliest and M/c sign.
- Demineralization & shallowing of the floor of sella turcica, with loss of its normal sub-cortical bone (White line)
- Erosion of the posterior clinoid process.
- The beaten-silver appearance.

PVL (Periventricular Leucomalacia)

- M/c ischemic brain injury seen in preterm infants.
- Ischemia is seen in border zone at the end of arterial distribution (White matter is affected)
- 60- 100 % infants develop spastic diplegia.

Calcification of intracranial structures

Physiological Calcification in Skull X-ray

- Choroid plexus
- Pineal gland in elderly
- Petroclenoid ligament
- Falx cerebri
- Lateral edges of diaphragm sellae

Basal ganglia Calcification

- Idiopathic with age (m/c cause)
- Hypoparathyroidism (2nd m/c)
- Lead & CO poisoning
- Wilson's ds
- Cysticercosis

Calcification in CT skull/Head

Calcification type	Condition
" Tram track"	Sturge Weber's
"Soap bubble"	Neurospargmiosis,
Rice grain	Neurocysticercoses
B/l symmetrical, stippled, periventricular	CMV
Ribbon like/dense nodular	Oligodendroglioma
Diffuse nodular(multiple scattered) flecks like	Intrauterine Toxoplasmosis
Sun ray calcification + spicules	Meningioma
Suprasellar , arc like	Craniopharyngioma
Bracket	Corpus callosum lipoma

Neoplasms showing Calcification

- Craniopharyngioma (Common)
- Oligodendroglioma
- Medulloblastoma
- Meningioma
- Papilloma of choroid plexus
- Pinealoma
- Chordoma
- Dermoid, epidermoid, teratoma, lipoma
- Astrocytoma

- M/c cause of intracranial calcification --- Pineal calcification.
- Tram line (Rail road) calcification is seen in Sturge Weber's syndrome.
- Type I (classic) lissencephaly with agyria can appear as the classic hour glass or figure-8 sign.

Ring enhancement on contrast CT (CECT)

- Toxoplasmosis
- Cysticercosis
- Tuberculoma
- Brain abscess
- Glioma metastasis
- Giant aneurysm
- Craniopharyngioma

Head injury and hematoma on CT

	Epidural	Subdural	SAH
Cause	Middle meningeal artery injury	Injury to cortical bridging veins	Berry aneurysm rupture
Crosses	Across dural attachment sutures	Do n't cross sutures	-
CT Scan	Biconvex	Crescent (Cocavo-convex)	NCCT (Non contrast CT) is investigation of choice
Other	2/3 hyperdense, 1/3 mixed appearance	1. Hyperdense (<2 wk) 2. Isodense (2-4wk) 3. Hyodense (>4 wk)	Four vessels (Both carotid & both vertebrals) DSA is IOC for determining etiology
			Hallmark of SAH is blood in CSF detected by LP.

ENT/NECK

Calcification of Pinna

- Ochronosis, Gout
- Frost bite
- Addison's ds
- Cockayne's syndrome

Thyroid nodule

- **USG findings s/o thyroid carcinoma in thyroid nodule:**
 - **Hypo-echogenicity**, microcalcifications, internal vascularity, irregular margins
 - Hyperechogenicity on USG of a thyroid nodule is more suggestive of thyroid cyst or a benign lesion.
 - Posterior indentation on Ba -swallow can be d/to aberrant right subclavian artery.

THORAX

The Silhouette Sign

Silhouette sign is used mainly for localizing intrathoracic lesion. Silhouette or structures of heart produce sign because of their contact with lung.

Sign

Produced in lesion of

Ascending aorta (Or Upper Rt heart border)	-- Ant. segment of RUL
Obscured Rt heart border	-- RML (ant. segment) lesion.
Obscured Lt heart border	-- Lingula / LLL
Descending aorta	-- Sup. & posterobasal segment of LLL
Hemidiaphragm	-- Basal segments lower lobes.
Upper Lt heart border	-- Ant. segment of LUL
Aortic knob/knuckle	-- apico-posterior segment of LUL

Hilum overlap sign

Differentiates b/w **anterior mediastinal mass** (which overlaps main pulmonary artery) & cardiac enlargement / Pericardial effusion .

Cervico-thoracic sign

Used in localizing **superior mediastinal lesion** in CXR PA view

- Ant. mediastinal lesion ---projects below the clavicle
- Post. mediastinal lesion ---- projects above the clavicle.

Hilar Shadow

Formed by lower lobe branch of pulmonary a. + Upper lobe veins (but NOT by bronchi) ??

Kerely Lines

- Kerely **A** lines : Seen in Apex
- Kerely **B** lines : Base. Interlobular septal lines which represent dilated lymphatics. Seen in pulmonary edema d/ to chronic pulmonary venous hypertension.
- Kerely **C** lines: In mid portions (Centre)

Cardiogenic pulmonary edema

- **Stage 1**: PVP 10-20 mmHg . Dyspnoea+
- **Stage 2**: PVP >20 mmHg . Kerely B lines +, tachypnea
- **Stage 3**: PVP >25 mmHg, bilateral rales/crepts, CXR shows "Batwing/ground -glass appearance".

Radiological features of LVF

- Cardiac enlargement
- Pulmonary venous hypertension :Stage3
bilateral haze/ground glass appearance, pleural effusion.

Important Radiological features of imp. CVS diseases:

- ASD --- Hilar dance on fluoroscopy
- ECCD --- Goose neck sign
- VSD --- Shunt vascularity
- TOF --- Heart size normal but marked RVH, 'Coeur en Sabot' or boot-shaped heart
Marked pulmonary oligemia
- TGA (uncorrected) --- 'Egg on side' or egg on string appearance on CXR
- Co A --- LVH, usually B/L notching of ribs inferior surface (4th-8th). Unilateral rib notching may be seen in pre subclavian type.
Inverted 3 sign (Figure of 3 or reversed 'E' sign) on Ba-studies.
- MS --- LAH, straightening of left heart border. 'Antler' or 'Moustache sign'
Double atrial shadow on X-ray
- Pericardial effusion --- 'Leather bottle' appearance of heart. Heart is pear shaped/ money bag/purse like
- TAPVC :
Non- obstructive --- Cardiomegaly, plethoric lung fields. "Snowman or figure of 8" appearance on CXR

Obstructive type --- Normal sized heart and
Ground glass appearance of lung fields d/to severe pulmonary HTN.

- Ebstein's anomaly --- Box shaped heart
- PAPVC --- Scimitar sign
- Carcinoid syndrome --- Calcified heart
- Pulmonary embolism --- Hampton hump, West mark's sign, Palla's sign.

- LAE (Left atrial enlargement)

Has four characterisitic features:-

- Double atrial shadow
- Straight left heart upper border,
- An elevated left mainstem bronchus,
- Posterior displacement of the cardiac silhouette.

→ Lambda sign is d/to small ascending aorta in hypoplastic left heart syndrome.

Sign/Finding	Seen in
Double atrial shadow	Left atrial enlargement, MS
Double aortic shadow in CXR	Aortic dissection
Double aortic arch	TOF, VSD, TGA

Imaging of Heart

- Reversible ischemia is detected by --- Thallium scan
- Fate of myocardial ischemia:
 1. Irreversible damage → infarction .
^{99m}Tc scan is used for infarct avid imaging .Hot spots are detected
 2. Chronic ischemia → persistent ischemic dysfunction
→ Hibernating myocardium .
Hibernating myocardium is viable and PET -scan (using NH₃ or rubidium 8) is gold standard for detection of viable myocardium/perfusion of heart. Recovery of contractile function is possible after successful revascularization.
 3. Relieved of ischemia → transient post ischemic dysfunction → Stunned myocardium
- Low dose ionotropes may be used in hibernating myocardium.
- Thallium (Tl²⁰¹) is agent used for myocardial perfusion studies. **Imaging agent of choice to assess myocardial viability.** Shows "Cold spot" in MI on perfusion scan (in Non avid infarct imaging)

Functional cardiac imaging

Radio isotope	Detects	Used for
Thallium scan	Reversible myocardial ischemia	Myocardial perfusion studies, viability
Thallium (Tl-201) (< 12-48 hr post infarct)	Cold spots	Myocardial infarcts (non-avid infarcts imaging)
Tc-99m pyrophosphate (> 10-12 hr post infarct)	Hot spot in MI	Infarct avid imaging
Tc-99m albumin	Ventriculography	Myocardial function

Neonatal Cyanosis

With Oligemia + Cardiomegaly	With oligemia, no cardiomegaly	With pleolemia (plethora)
(All have an ASD)	(Sign appear usually after 1 wk)	Cyanosis + CCF
<ul style="list-style-type: none"> PS Pulm atresia Ebstein anomaly Tricuspid atresia 	<ul style="list-style-type: none"> TOF Pulm atresia with VSD Tricuspid atresia 	<ul style="list-style-type: none"> TAPVC Hypoplastic LV Interrupted aortic arch TGA Truncus arteriosus

Ribs

- Flaring of anterior end of ribs is seen in --- Rickets.
- Beaded ribs are seen in --- Osteogenesis imperfecta.
- Causes of multiple anterior rib flaring --- Achondroplasia, scurvy, thanatophoric dysplasia, normal variant.

Metastasis in Lung

Calcifying	Cavitating	Hemorrhagic lung metastasis with ill defined nodules
<ul style="list-style-type: none"> Breast Osteosarcoma/ chondroma Thyroid (papillary) Mucinous adenoca Lung metastasis following RT/chemo Testicular, Ovarian 	<ul style="list-style-type: none"> SqCC, Sarcoma Colon Melanoma Transitional CC Cx under CT Chemotherapy 	<ul style="list-style-type: none"> Choriocarcinoma RCC Melanoma Thyroid Ca

Miliary Shadows on CXR

CWP & Silicosis, MS, Sarcoidosis, Hyperparathyroidism, Eosinophilic granuloma (Histiocytosis X), Blastomycosis, coccidiomycosis, Histoplasmosis, Streptococcal pneumonitis, VZV (But not in staphylococcal d/s)

White out lung D/d

Trachea pulled toward the opacified side	Trachea remains central in position	Pushed away from the opacified side
Pneumonectomy	Consolidation (Lobar)	Pleural effusion
Total lung collapse: e.g. endobronchial intubation	Pulmonary edema / ARDS	Diaphragmatic hernia
Pulmonary agenesis/hypoplasia	Chest wall mass: e.g. Askin / Ewing sarcoma	Large pulmonary mass

Pneumomediastinum

Hamman's sign +ve

- Lung tear
- Asthma
- Artificial ventilation
- Esophageal perforation
- Spontaneous (MC cause)
- Diabetic ketoacidosis
- Histiocytosis
- Resp. distress syndrome

Hydatid cyst of Lung

- Oval mass, almost never calcify.
- Meniscus/moon sign (air crescent of mycetoma/double arch sign)
- Cumbo sign (air filled levels)
- Waterlilly/ Camalotte sign
- Serpent/rising sun sign
- Empty cyst sign

Egg shell calcification in LN

Peripheral rim calcification esp. of hilar lymph nodes

- Characteristic of silicosis (m/c cause) & sarcoidosis
- Histoplasmosis, coccidiomycosis, TB
- Lymphoma (post RT)
- CWP, fibrosing mediastinitis (PMF)

[Remember: Egg shell calcification is NOT seen in Asbestosis, Berylliosis, Ca-lung]

→ Tuberculosis is the m/c cause of necrotic lymph node with peripheral rim enhancement. B/L upper lobe fibrosis may be seen.

→ Lymphoma is characterized by non-necrotic potato nodes.

→ Post pneumonia calcification is seen in - Chicken pox

→ Bibasilar reticular or (reticonodular) pattern is seen in ILDs

→ PCP in AIDS is characterised by b/L diffuse infiltrates beginning in the perihilar region (ground glass app.)

Perihilar fluffy opacities/Bats wing/Butterfly appearance

- Pulmonary venous HTN
- SLE
- Herpes
- AIDS

Calcification in Lungs & Pleura

Calcification in lungs	Pleural calcification
○ B/L in TB	○ Old empyema/hemothorax
○ B/L Histoplasma	○ Talc exposure
○ B/L coccidiomycosis	○ Asbestosis, silicosis

Cardiac Calcification

Intracardiac	Myocardial	Pericardial
○ Atrial myxoma	○ Mainly in LV-apex	○ Mainly in right chambers (RV) & A-V groove
○ Valve thrombus	○ Post myocarditis	○ Constrictive pericarditis
	○ Hydatid ds	○ Post-traumatic
	○ aneurysms	○ Uremia / CRF
	○ Infarct	○ Asbestosis

Findings in Pulmonary HTN

- Pruning of vessels
- Hilar shadows
- RVH
- Pulmonary bay

ABDOMEN

Bowel in intestinal obstruction in erect films

Obstruction of organ	Radiological Features
○ Small bowel	Straight segments that are central and lie transversely (no gas in colon/Colon cut-off sign), string of beads
○ Jejunum	Vulvulae conniventes
○ Ileum	Featureless
○ Caecum	Rounded gas shadow in right iliac fossa
○ Large bowel	Haustral fold spaced irregularly

Small intestine is differentiated from large intestine by-

<u>Small intestine</u>	<u>Large intestine</u>
Central location	Peripheral
Vulvulae conniventes	Haustrations
Diameter 2.5-3 cm	Diameter >5cm

→ In intestinal obstruction, fluid levels appear later than gas shadow as it takes time for gas and fluid to separate.

→ Coffee bean sign is seen in strangulation of incompletely obstructed loops of small intestine.

→ In the small bowel, the number of fluid levels is directly proportional to the degree of obstruction and to its site, the number increasing the more distal the lesion

→ Best investigation to visualise small intestinal pathology--- Barium meal follow through > enteroclysis.

→ Imaging modality of choice for partial small bowel obstruction--Barium meal follow through (BMFT)

→ Microcolon in barium enema suggests--- obstruction proximal to ileocecal valve.

IMP.FINDINGS :CONTRAST X-RAY ABDOMEN

Barium Swallow

Condition	Ba-swallow Features
○ Achalasia cardia	Bird's beak deformity of lower esophagus
○ Ca esophagus	Rat tail tapering of lower esophagus
○ Diffuse esophageal spasm	Corkscrew esophagus

Barium Meal

Condition	Ba-meal Features
○ Gastric carcinoma	Filling defect in antrum/body (On barium meal follow through)
○ Chronic duodenal ulcer with scarring	Trifoliate duodenum
○ Leiomyosarcoma	Bull's eye lesion
○ Idiopathic HPS (hypertrophic pyloric stenosis)	String sign
○ Carcinoma head of pancreas	Antral Pad sign, Wide C-loop of duodenum (Sign of Frostberg)

Barium Enema

Condition	Radiological signs on Ba-enema
○ Small bowel obstruction	String of beads
○ Ileocecal TB	Pulled up contracted caecum, obtuse ileocecal angle, filling defect, incompetent ileocecal valve (Fleischer sign/ Inverted umbrella defect)
○ Crohn's disease	String sign of Cantor
○ Intussusception	Coiled spring sign, pincer shaped ending
○ Ischemic colitis	Thumb printing sign
○ UC	Loss of haustrations, "lead pipe" or pipe stem appearance
○ Colonic polyps	Smooth regular filling defect
○ Ca colon	Irregular filling defect, "Apple core deformity"
○ Diverticulosis	"Saw - tooth appearance"

ERCP & X-Ray in Pancreatitis

Condition	ERCP findings	X-ray abdomen
○ Acute pancreatitis	Calculi, blocked duct, Dilatation & beading of main panc. duct, cavities	"Colon cutoff" sign, sentinel loop, Gasless abdomen, Renal halo sign
○ Chronic pancreatitis	Beading, chain of lakes, string of pearl appearance, Rat tail stricture of CBD	Irregular calcifications
○ Carcinoma pancreas	Double duct sign, scrambled egg appearance	Inverted 3 sign of frostberg, widening of C-loop of duodenum (pad sign/Rose thorning)

- Sunburst calcification on plain X-ray is seen in - Insulinoma
- Spongy appearance with central sunburst calcification is seen in serous cystadenoma or microcystic adenoma of pancreas.

Air Bubble signs in Neonate

- Single bubble sign --- In pyloric stenosis
- Double bubble sign --- In duodenal atresia/stenosis, Ladd's band/ malrotation, annular pancreas
- Triple bubble sign --- In jejunal/ ileal atresia

Gasless Abdomen on X-Ray

- Acute Pancreatitis, annular pancreas
- Malrotation of gut pyloric stenosis, duodenal atresia
- Congenital diaphragmatic hernia
- Mesenteric infraction

Microcolon is seen in

- Meconium ileus
- Ileal atresia
- Total Colonic aganglionosis [Mnemonic : Mic]

Benign Vs Malignant Gastric Ulcer

	Benign	Malignant
○ Age group	Young	Old
○ Location	On lesser curvature	Greater curvature
○ Margins	Beaded/heaped up but not elevated	Beaded/ heaped up, elevated
○ Base	Smooth, clear	Shaggy, necrotic
○ Mucosal fold	Radiate spoke like	do not reach the edge
○ Sign	Ulcer mound hampton's line, penetrating sign	Carman's meniscus sign, Kirkland complex, Intraluminal crater

Radiological Features of GI conditions

Ileal Atresia

- Multiple air fluid levels in plain X-ray.
- Obstruction in Ba- meal
- Microcolon in Ba- enema
- Apple peel appearance

Diverticulosis

- "Saw teeth" appearance and 'champagne glass' sign.

Volvulus

- "Coffee Bean Sign", tyre tube appearance on plain X-ray
- "Bird's Beak" sign – Tapered hook like end of barium colon; Ace of spades and Omega sign on Ba enema
- On CT scan
Whirl sign (tightly torsioned mesentery formed by twisted afferent and efferent loop)

Intussusception

- "Claw sign"/ coiled spring sign (Barium enema)
- Pseudokidney sign / Bull's eye / Target sign (USG)
- Multiple air fluid levels (X-ray plain abdomen)

Hirschsprung's Disease

- Dilatation of large and small bowel abnormally from transitional zone
- Marked retention of barium on delayed films.

Cholecystitis

- *Acute*: Circumferential halo of low echogenicity around GB. Mural thickening of >3 mm in fasting state. Calculi, echogenic bile.
- *Chronic*: Contracted GB, obliteration of lumen.

Adenomyomatosis of GB

- Thickened wall.
- Pearl necklace GB.
- Comet tail artifact b/w cholesterol crystals in RA sinus is pathognomic.

Air in biliary tract is seen in

- G.I. fistula (e.g. in trauma, malignancy, gallstone ileus)
- Emphysematous cholecystitis
- Reflex of duodenal gas (biliary ascariasis, surgical patient)

GB thickening on USG is seen in

- Cholecystitis, cholesterosis, adenomyomatosis
- Ascites, portal HTN, hypoalbuminemia, CCF liver cirrhosis, vital hepatitis,

- Central dot sign on USG is seen in --- Caroli's d/s (Type V choledochal cyst)
- Comet tail sign on USG is seen in --- Adenomyomatosis, abscess, air in bile tree

→ USG is the IOC for gall stones.

→ Porcelain GB is seen in --- carcinoma GB

→ Napkin ring sign is seen in annular carcinoma of colon.

GUT

IVU/ IVP Findings

Indication	IVP / Radiological Finding
◦ Hydronephrosis	Clubbing of calyces, Crescent sign (cortex compressing ureteric & pelvic diameter)
◦ Congenital anomalies	
1. Horse shoe kidney	Flower vase appearance of ureter
2. Ureterocele	Adder / cobra head appearance
3. Polycystic (PKD)	B/L Spider leg appearance
4. Retrocaval ureter	Reverse 'J' sign with hydronephrosis
5. Ectopic ureter	Drooping flower appearance
◦ BPH	Fish hook bladder
◦ Chronic/tubercular cystitis	Thimble bladder
◦ RCC	Irregular filling defect, u/L spider leg appearance
◦ Acute arterial renal occlusion (RVT, ATN)	Rim nephrogram
◦ Cortical necrosis	Reverse rim sign

- Radiological findings of papillary necrosis on excretory urogram :-

- 'Egg in cup' appearance
- Ring shadows ,
- ↓ed dense nephrogram,
- Tract & horn from calyces.

Isotope Scan

• DTPA

- Its excretion rate measures GFR
- Useful to study renal Perfusion, functions of each kidney

Dynamic radionuclide renography (e.g. DTPA renogram) is safest and simplest way to assess renal perfusion in patient with renal failure. It is IOC in a patient with ARF with complete anuria.

Dense renogram c/b seen d/to dehydration of patient.

• DMSA

Useful to assess cortical functions & anatomy of kidney

- *Rapid sequence urography is carried out in patients with suspected renovascular hypertension.*
- *Urethroscopy is confirmatory for stricture of urethra.*
- *Infusion urography – compromised renal function.*
- *Diuretic urography – PUJ obstruction.*
- *Micturating cystourethrography (MCU)/ Voiding cystourethrogram – VUR and posterior urethral valve.*
- *Retrograde urethrogram is best – to visualise anterior (penile) urethra.*

BONES/ X- RAY HANDS

No. of Carpal bones in X-ray of a child

6 mth	1yr	2yr	3yr	4yr	5yr	6yr	12yr
0	2	2	3	4	4	7	8
	(H+C)						(All bone appear)

Important Findings in X- ray Hand

Disease	Findings	Other/f
Hyperparathyroidism	Subperiosteal erosion of radial aspect of middle phalanx + Tufting	Brown tumour, salt & pepper skull
Pseudohypoparathyroidism	Markedly short 4 th metacarpal	Atrophy of 4 th & 5 th metacarpal bones
Acromegaly	Arrow head distal phalanx	↑ heel pad thickness
Psoriatic arthropathy	Tufting of distal phalanx (d/to new bone formation), sausage digits, Gull's Wing app.	DIP, MCP involved

RICKETS VS SCURVY

Disease	Scurvy	Rickets
• Classical X-ray changes	Knee 1. White line of Frankel 2. Corner sign (d/t periosteal infarct) 3. Groundglass appearance 4. Subperiosteal hematoma, elevation of periosteum 5. Pelkan spur d/t metaphyseal #	Wrists 1. Widening (double malleoli) 2. Cupping (Saucer like depression) 3. Flaring (champagne glass app.) 4. Fraying (rarefaction)
• Epiphysis Pseudo-hypoparathyroidism	Signet ring	↑ distance b/w epiphyseal centre & growth plate
• Physis (Growth plate)	NARROW	WIDE
• Rosary	Scorbutic Tender, step shape, sternum depressed	Rachitic Non- tender, smooth rounded cc junctions
• Other/f	Trummer field zone (fragmented metaphysis) Wimberger/Halo sign Pencil thin cortex Pseudoparalysis	ZPC (zone of preparatory calcification) on t/t Pectus carinatum Harrison's sulcus/groove
	Osteoporosis	Green stick #, bowing

• Healing in rickets :

Indicated by the zone of preparatory calcification (ZPC). As the healing progresses the osteoid tissue become calcified and shaft grows towards the line of ZPC until it becomes united with it. Healing changes are best demonstrated in wrist in crawling child, and in knee in the child who walks.

• Scurvy :

Child with frog like position (pseudoparalysis) & resistance to move limbs (tender limbs d/to hematoma) are seen in scurvy. Scurvy is d/to defective formation of osteoid matrix. Vitamin C deficiency causes impaired synthesis of collagen resulting in bleeding tendencies, impaired wound healing, poor vascular support.



Photograph: X-ray wrist in Rickets



Photograph: A Child with Rickets

Grossly expansile lucent bone lesions

- Aneurysmal cyst
- Enchondroma
- Osteosarcoma
- Giant cell tumor
- Fibrous dysplasia
- Plasmacytoma
- Hemophilia
- Brown tumour (Hyperparathyroidism)

→ *M/c cause is secondaries from RCC & papillary carcinoma of thyroid*

Moth eaten appearance of bone is seen in -

- MM
- Lymphoma
- Sarcoma
- Osteomyelitis
- Leukemia
- Histiocytosis -x

Enlargement of Epiphysis

- JRA
- Rickets
- Hemophilia
- TB, fungal Arthritis

→ *Enlargement of epiphysis is characteristic of--- JRA.*

→ *Epiphyseal dysgenesis is characteristic of--- hypothyroidism.*

→ *Widening of physis (epiphyseal growth plate) is seen in--- rickets*

→ *Epiphyseal loss of density is seen in--- scurvy*

Osteopenia is seen in

- With normal skeletal maturation ---Rickets, hypoparathyroidism, Cushing's
- With delayed skeletal maturation ---Hypothyroidism, Addison's

Causes of Floating teeth

- Langerhans cell histiocytosis
- Hyperparathyroidism
- Metastases
- Multiple myeloma
- Lymphoma/leukemia

Bone secondaries

- Bone is a common site of metastasis for carcinoma of prostate, breast, lung, kidney, bladder and thyroid and also for lymphoma and sarcomas.
- According to CSDT order of frequency of primary carcinoma metastasising to bone is – **breast > prostate > lung > kidney > thyroid > pancreas / stomach**
- Tumours usually spread to bone hematogenously (BM metastasis), but local invasion from soft tissue may occur
- Sites of bone involved from secondary in descending order – **vertebrae > proximal femur > pelvis > ribs > proximal humerus > skull**
- Pain is the most common symptom of bony metastases
- Most common primary source of solitary skeletal metastasis at the time of diagnosis is – RCC
- Therefore, an IVP should be part of prebiopsy workup of solitary metastases with no obvious primary
- Best investigation for bony metastases is bone scan.

Majority of the bone secondaries are osteolytic, but few can be osteoblastic as Carcinoma of the prostate in males and carcinoma of breast in females are the commonest tumour to give rise to sclerotic secondaries in the bone.

- Mostly blastic --- Prostate, carcinoid
- Usually lytic but frequently blastic --- Breast
- Invariably lytic --- Kidney, thyroid
- Rest are mixed type

→ *Vertebral bodies are most frequent site. Other sites are ribs, pelvis and femur.*

→ *M/c symptom is bone pain in the spine. Pathological fracture are common in spine.*

→ *Secondaries in the bone are uncommon distal to the elbow and knee.*

VERTEBRAL COLUM/SPINE

Important findings vertebrae/ spine

- Picture frame vertebrae --- In *Paget's ds*
- Cod fish (biconcave) vertebrae --- Osteomalacia, osteoporosis, hyperparathyroidism
- Fish mouth vertebrae --- SCD, homocystinuria
- Calcification of IVD --- Alkaptonuria (ochronosis)
- Vertebrae plana --- Eosinophilic granuloma

→ *Rugger jersy spine is X-ray app. d/to sclerosis of upper and lower spinal borders seen in osteopetrosis, CRF induced osteomalacia, renal osteodystrophy.*

→ *Striated vertebral bodies with Corduroy appearance on CT is seen in hemangioma of spine (vertebrae). Also k/as accordion/ Polka dot/ honey comb appearance.*

Calcification of IVD is seen in

- Alkaptonuria (ochronosis) --- m/c cause
- AS, degenerative spondylosis
- Pseudogout (CPPD deposition disease)
- Gout
- Hemochromatosis
- DISH

Intervertebral disc space

- M/c cause of single vertebral body collapse in a child with

intact disc space is eosinophilic granuloma (single vertebrae plana)

- In metastasis --- disc space is preserved until late. Common in elderly, involves multiple vertebrae
- In Pott's ds (TB spine) --- ↓ disc space is the earliest sign in paradiscal type.
- IVD space is usually normal or maintained in trauma, eosinophilic granuloma, metastases, osteoporosis.

→ *Myelomalacia (cord atrophy) is the end stage of cord trauma (hyperintense on T2W1 MRI)*

RADIOLOGICAL CHANGES IN SOME D/S

SCD (Sickle cell d/s)

- Hair on end straitions.
- Coarse trabeculae (d/to marrow hyperplasia).
- Endosteal opposition of bone leading to bone within bone appearance.
- Bone infarcts in
 1. Long bones : Collapsed femur head.
 2. Spine : H-shaped depression of vertebrae (Vertebra plana)
- 2^o osteomyelitis : Salmonella infection.

Langhan's cell Histiocytosis

- Vertebra plana with intact disc space.
- Punched out lucencies in skull vault coalesce to form geographical skull.
- Floating teeth

Spina bifida (USG findings)

- M/c in lumbosacral region.
- Banana sign (Cerebellum is stretched around brain stem)
- Lemon sign (Flattening of frontal bones on transverse image)
- Bony defect in spine.
- Presence of intact sac on post^r spine, which is filled with fluid (meningocele) or solid tissue (myelomeningocele)
- V-shaped profile.

Leukaemia & metastatic Neuroblastoma in childhood.

- Metaphyseal translucencies (earliest & most characteristic sign is +nce of dark band running across the metaphysis below growth plate.)
- Metaphyseal cortical erosion

- Metaphyseal osteosclerosis
- Periosteal reaction & new bone formation
- Osteolytic lesions (commonest in shaft of long bones)

X-Ray features of splenic injury are

- # of left lower ribs
- Obliteration of splenic & psoas shadow
- Elevation of left hemidiaphragm
- Indentation of stomach & presence of free fluid in b/w coils of intestines are suggestive of splenic rupture.

RADIATION : BASIC CONCEPTS

Ionizing Radiation:

- There are two types of ionizing radiation:
 1. Electromagnetic radiation (photons)
 2. Corpuscular/particulate radiation
- *Electromagnetic radiation* includes:

Waves - like Radio, heat, light, UV, X-rays & γ rays
- *Corpuscular radiation* includes:

Particles - like electrons, protons, neutrons, mesons, alpha(α) beta(β), heavy ions
- *Radiological procedures which can produce ionizing radiation:*

X-ray, Fluoroscopy, DSA, SPECT, PET, CT, nuclear scans
CECT etc

Characteristics of α , β , γ and X-rays.

Property	α	β	γ	X-rays
Nature	${}_2\alpha^4$ or ${}_2\text{He}^4$	${}_1e^0$	${}_0\gamma^0$	EM waves
Source	Nucleus	e^-	Nucleus of an atom	Orbital electron
Charge	+2	-1	0	
Mass	4 unit	9.31×10^{-31} kg (almost 0)	0	
Velocity	$C/10$	0.9 C	$C (3 \times 10^8 \text{ m/s})$	C
Penetrating power (Penetrates Al sheet of)	+	++	++++	+++
	(0.002 cm)	(0.2 cm)	(100 cm)	(50 cm)
Ionizing/Damaging power	10,000x	100x	x	—

- Maximum penetration power --- γ -rays > X-rays.
- Maximum ionizing power, Max^m damage to DNA --- α -rays
- Source of radiation that causes heat cataract—*infrared radiation*
- Principle used in radiotherapy is --- *Ionization of molecules*
- Functional basis of ionizing radiation is --- *Excitation of electrons from orbit*
- Oxygen enhancement ratio is max^m with neutrons.

- Alpha radiation consists of helium-4 (${}_2\text{He}^4$) nuclei and is readily stopped by a sheet of paper. Beta radiation, consisting of electrons, is halted by an aluminium plate. Gamma radiation is eventually absorbed as it penetrates a dense material.

Source of radiation c/b broadly divided into

1. *Natural (background) radiation* : Present in the earth all the time. It can be cosmic, terrestrial or internal radiation. **K-40** is the biggest contributor to internal body radiation.
 2. *Man made (artificial) radiation* : All other forms of radiation.
- **Densely ionizing radiation** include α -particles & heavy ions while **sparsely ionizing radiations** are X-ray & γ -rays.
 - *Primary radiation* : Which emerges from the tube & reaches patient.
 - *Secondary radiation* : radiation which scatters on contact with the patient.

Radiation Sources

- γ -rays --- emitted by Cs, Tc, Ra, I^{131} , Co
- α -rays --- emitted by U-235, P_4 -239, Th 232
- β -rays --- emitted by P-32, Sr-90, Co, Cs, I^{131} , Tc, Y-90, Au
- Both β & γ rays are emitted by --- **I-131** (mainly $\beta > \gamma$), Ra, Au
- **Neutron emitting Radioisotope** --- Californium
- *Tissue penetration capability*

γ -ray > X-ray > β -ray > α -particle
(50cm) (15-30 cm) (.06 - 4 mm) (.05 mm)

- Radioisotope capable of displacing calcium from body is Strontium
- C^{14} is used for carbon dating.
- The m/c form of irradiation is by use of external beam photons or electrons. Photons are x-rays or γ rays.
- The modern radiotherapy unit, linear accelerator produces both X-rays and electrons
- Smaller the wavelength (λ), or the higher the frequency, the higher will be the energy of photon.
- Cr^{51} and CO (carbon mono-oxide) are used to determine total volume of red cells in the body.

Electromagnetic (EM) Radiation/ waves

- The spectrum of waves propagated through space or matter by the oscillation of electric field and a magnetic field at right angles to one another (waves travel perpendicular to both electric and magnetic fields)
- Have **velocity of 3×10^8 m/s in vacuum (= C)**
- Waves in *decreasing order of wavelength*.
Radio waves > microwaves > infrared > visible (VIBGYOR)
> UV- rays > X-rays > γ -rays > cosmic rays.
[MNEMONIC ---RMIVUXG]

UV-rays

- Electromagnetic waves
- Uses :
 - In Wood's lamp : 340- 450 nm (Peak at 365 nm) d/g of skin disorders.
 - In phototherapy :
 - In t/t of psoriasis
- Hazards :
 - Photophthalmia (Snow blindness)

X-ray and gamma rays:

- X-ray & gamma rays are 2 forms of EM radiations which are similar in nature and properties.
- For X-rays & gamma rays the events are well separated in space & so these radiations are said to be "*sparsely ionizing*". They have no charge and mass and are unaffected by the magnetic field.
- The only difference b/n X-rays & gamma-rays is in their origin. X-rays are produced from orbital electron whereas γ -rays are produced from the nucleus of an atom.

X-ray and visible light rays:

- X-rays differ from light in wavelength . X-rays are EM radiation of very short wavelength of few nm range.

- Visible light spectrum has higher wavelength (400- 700 nm range). Wavelength of X-rays is $1/10,000$ of that of the light rays, i.e. 7.5×10^{-6} - 1.7×10^{-9}
- Frequency and wavelength are inversely related (e.g. γ -rays and X-rays have very high frequency & they have very short wavelength.)
- Neutrons (n^1) are uncharged particles with variable penetration power .
- Alpha particles are positively charged heavy particles with less penetrating power.

X-rays

- X - rays are EM waves.
- X - rays are produced when fast moving stream of electrons (produced by beam of high speed cathode rays) strikes the anode made of tungsten (thermionic emission).
- Target is made up of molybdenum in mammography
- Linear accelerator (Linac) and betatron are used to produce X-rays by accelerating electrons.
- Cyclotron is used to produce γ -rays.
- Microtron combines principles of both linac +cyclotron.
- Simulator uses a diagnostic X-ray tube but duplicates a radiation t/t. Used to display t/t fields.
- X-rays with higher accelerating voltage have higher rate of emission of e- from filament (thermionic emission), higher speeds of striking electrons, high energy & more penetration power [Energy (E) = $v/d = hv = hf$]
- They have higher frequency, greater power of penetration, high energy than particles
- X-rays are most scattered by H^+ ion. (Scattering depends upon electron/ nucleus ratio)
- Now a days X- rays are produced by cooling tube
- Target is made up of molybdenum in mammography (not of tungsten)
- Betatron can provide X-rays & electron therapy beams over a range of 2 MeV to ≥ 40 Mev.

Properties

- The X-ray beam has two main properties
 - 1) Beam quality is the ability of the beam to penetrate an object, its all about the penetrating power of the X-ray photons, this is controlled by the KVP control.
 - 2) Beam intensity (Quantity) this is the number of X-ray photons in the beam and is principally controlled by the mA (tube current).

But note as you increase the KV not only does the quality harden (more penetrating) but you do actually get more photons so intensity increases too.

• **kVp (Kilo volt peak):**

Voltage is the components which controls **quality** of X-ray. The energy (or the penetrating power) of the x-ray beam is controlled by the voltage adjustment. This control usually is labelled in keV (thousand electron volts) and sometimes the level is referred to as kVp (kilovoltage potential). The higher the voltage setting, the more energetic will be the beam of x-ray. A more penetrating beam will result in a lower contrast radiograph than one made with an x-ray beam having less penetrating power.

Penetrating power \propto kVp

• **Current mAS (Mili ampere seconds):**

Determines the **quantity** of X-ray and the radiation dose.

• **S Time**

The third control of the X-ray tube which is used for medical imaging is the exposure timer. This is usually denoted as an "S" (exposure time in seconds) and is combined with the mA control. The combined function is usually referred to as *mAs* or *milliampere seconds*. If you want to double film blackness you could just double the mAs.

• **Distance b/w X-ray tube & patient follows inverse square law**

$$\text{Radiation intensity} \propto \frac{1}{d^2}$$

• **Contrast** is inversely related to KVp. Contrast is \uparrow by \downarrow in KVp. Image contrast is controlled by the energy of the "x" photon beam. Therefore, high kV techniques result in low contrast images

• **Penetration** is \uparrow by \uparrow in KVp. Obese/ heavily built patient require \uparrow in KVp.

• **Density.** Is the degree of blackening of the film after processing. High density means over exposed. X-ray. in X-ray depends upon : *kVp & target film distance*.

• **Use of filter** result in production of *beam of greater intensity*. Filter are made up of Al-Cu combination. They absorb low energy X-rays and \downarrow patient's exposures.

• **Grid:** M/c method of reducing scatter is to use a radiographic grid. It is composed of alternating radiopaque (lead) and radiolucent (aluminum) strips. The use of this radiographic grid will greatly improve image sharpness when a relatively thick body part is being imaged.

• **Absorption :**

The degree of absorption depends on the density (atomic wt) of the matter. Dense tissues like the bone, absorb X-rays far more readily than do the soft tissues of the body. The thicker the subject the more absorption of x-rays so the thicker the part the more mAS you require.

• **Structures with increasing radio opacity are ---**

Air < fat < soft tissues m/s, vessels, viscera etc < bone < enamel < metallic foreign bodies

Effects

• **Photographic effect**

X-ray film is made up of *cellulose acetate*, coated on its both sides with silver bromide emulsion.

This emulsion is photosensitive & is responsible for P-effect.

• **Fluorescent effect**

When X-ray strikes mettalic salts like Zn, Cd, sulphides, the rays cause them to fluoresce.

• **Photoelectric effect**

Absorption of *low energy* from radiation in tissue leads to ionization & produces this effect. used in *diagnostic* radiology

• **Compton effect** --- d/to absorption of high energy, used in *therapeutic* radiology

• **Pair production** --- Seen at very high energy levels (in *accidental* X-ray leak).

• **Super voltage therapy** - X-ray therapy in the range of 500-1000 KV

RADIOISOTOPES

Ionizing radiations may be delivered clinically in three ways--

1. External beam irradiation
2. Brachytherapy
3. Internal/ systemic irradiation

1. Brachytherapy

- Radioactive sources are placed in close proximity to or directly into tumour.
- Brachytherapy means interstitial, intracavitary & surface application of radioisotopes
- *Imp. sources are*

Co-60, Cs-137, Ir-192, I-125

Radium -226 occurs in nature, its half life is 1626 years,

Co-60 produced by n- γ reaction in reactors from stable cobalt $_{27}\text{Co}^{59}$

Tantalum Ta 182 , Gold Au 198 , Radon Rn 222

	Interstitial	Intracavitary
Needles/seeds are placed into	Cancerous tissue (Prostate/ penis/ other soft tissue)	Cavity e.g. In urethra, in cervix
Sources	2 types Permanent implants Cs 131 , Au 198 , Ir 192 Temporary implants — Sr 90 , Cs 137 , Ir 192 , Ra 226 Radon 222 , Co 60 , γ^{169}	(M/c used Cs 137 in cancer of cervix)

2. Teletherapy (External beam RT)

- Radioactive sources are placed at a distance from the body (usually 80-100 cm)
- Was carried out with X-ray generated at voltage upto 300 KVP
- Broadly divided into
 - Kilovoltage therapy (superficial therapy)
T/t with X-rays produced at a energy ranging from 50-150 KV (1-6 mm aluminium filters are used)
 - Orthovoltage or deep therapy - t/t with X-rays ranging from 150 to 500 KV. Can filter 1-4 mm of copper.

2. Megavoltage therapy

- Electrons are used mainly for treating skin or superficial tissues
- Sources -M/c isotope used is Co 60 (emits gamma rays), ^{137}Cs and 4 MV linac, betatron
 - Radioisotope used in both teletherapy and brachytherapy Cs 137 > Co 60
 - Cs 131 is m/c used for permanent interstitial implants in brachytherapy

$T_{1/2}$ (Half life of radioisotopes)

$T_{1/2}$ in hours	$T_{1/2}$ in days	$T_{1/2}$ in years
I 132 2.3 hrs	Gold 2.7 days	Co 60 5.2 yrs
Tc 99 6 hrs	Thallium 3.2 days	Tritium 12yrs
	Gallium	St 90 28 yrs
I 123 13 hrs	Radon 3.8 days	Cs 137 30 yrs
	Xenon 5.2 days	Ra 1622 yrs
	I 131 8 days	U 701×10^8 yrs
	P 32 14 days	
	^{125}I 60 days	

- Maximum Half-life is of uranium 701×10^8 yrs > Ra (1622 yrs.)
- Radium is obsolete in radiotherapy becoz of longer $t_{1/2}$
- Radium emits α , β , γ rays and decays to radon

Manchester System

- Point A lies 2 cm lateral to the uterine canal and 2 cm above from the mucosa of the lateral fornix of the vagina in the plane of uterus
- Point B 5 cm from midline and 2 cm up from the mucous membrane of the lateral fornix. It represents the close full off in the lateral region and as well as the dose near the pelvic wall and obturator node. In cancer of cervix exposure dose of 8000R in 144 hours to Point A in 2 fraction (4000R/ 72 hr).

Radioactive P32 is useful in

- Diagnosis of : Eye cancers, Esophageal cancers
- R_x of : Sq CC, Ca esophagus, CML, MM, bone secondaries, Ca breast, Ca prostate, Polycythemia vera Malignant ascites, Mycosis fungoides, Senile keratosis, Superficial angiomias

Units of

- Radiation exposure --- Röntgen
- Radiation absorbed dose --- Gray & Rad [remember Red & Gray colors, 1 Gy = 100 Rads]
- Radioactivity --- Curie
- Radiation effectiveness --- Rem, Sievert (or public health measure of radiation)

- Measurement that defines the effect of radiation in the specific organ exposed -- Effective dose.
- Unit of biological effectiveness or dose equivalent --- Rem
- Dose equivalent measures the biological effect of radiation on the body as a whole
- Ed = Dose equivalent x weight factor

Radiosensitivity

	Most radiosensitive	Least sensitive or radioresistant
1. Stage of cell cycle	G ₂ M > M	S phase
2. Organ	Ovary, testis	Vagina (bone CNS, cartilage, muscle)
3. Tissue	Bone marrow, gonads	Nervous tissue (bone, CNS, cartilage, muscle)
4. Cell	Rapidly dividing	Quiescent
5. Blood	Lymphocyte	Platelet

- M/c mucosal surface affected is intestinal mucosa
- Among radioresistant vascular structures, most sensitive is vascular endothelium
- Among nervous tissues most sensitive is neuron
- M/c organ affected is skin and presents as erythema
- For Chemotherapy & radiotherapy induced cardiotoxicity investigation of choice is endomyocardial biopsy

→ Most sensitive

- Testicular tumour – Seminoma
- Ovarian tumour – Dysgerminoma
- Brain tumour – Medulloblastoma
- Lung tumour – Small cell carcinoma
- Skin cancer – Basal cell cancer
- Bone tumours – Ewing's sarcoma, multiple myeloma

Radiation Hazards

Acute Radiation Syndrome

- Haematopoietic syndrome develops earliest at 2 G or 200 cGy. A 50% ↓ in lymphocyte count indicates lethal exposure.
- G.I. syndrome – 5-12 Gy. death is earliest
- CNS syndrome – 1000 Gy
- Bone marrow damage – 250 rads

Radiation Protection

- Stochastic Effects: Probability of occurrence ↑es with ↑ in dose. e.g. cancer, genetic effects (Lower the dose lesser the chance)
- Radiation protection is done by barrier shielding design using lead (Pb) shields.
- Viewing window in CT room is made up of 1.5 mm lead equivalence.

Radiosensitizers	Radio-protective Agents	Radiation Potentiator
Chemotherapeutic agents which enhance radiation effect by sensitizing the cell (radio-mimetic)	Chemotherapeutic agents which protect the cell from radiation injury in tissues previously treated with radiation	They have been reported to cause flare-up of dermatitis / esophagitis in area (radiation recall reactions)
• Cisplatin	• Amifostine	• Doxorubicin
• 5-FU	• Sodium butyrate	• Dactinomycin
• Hydroxyurea		
• Vincristine		
• Metronidazole		
• Bleomycin (but NOT cyclophosphamide)		

- Amifostine reduces cisplatin-induced nephrotoxicity and xerostomia in a patient of head & neck cancer. Does not protect CNS and skin.

Protective lead aprons

- Are made up of lead impregnated with vinyl / Perspex within the range of 0.25-1.0 mm of lead equivalency
- Greater the lead equivalence, protection is more and weight of apron increases.
- Lead apron of 0.5 mm thickness will reduce the intensity of scattered X-rays >90% and should be worn by all workers
- Lead equivalence of aprons is 0.5mm (gonadal shield) and gloves is 0.25 mm

- Radiation exposure should not exceeds ≥ 5 rads/year.
- Maximum radiation dose permitted by ESI 5 rad.
- Diagnostic range of radiation i.e. <5 rads is not associated with teratogenic effect in human
- Lead apron (0.5 mm) is used to protect against radiation

Historical Aspect

- J.J. Thompson --- discovered electrons.
- W.K. Roentgen --- discovered X-rays in 1895.
- Henry Becquerel --- discovered radioactivity in 1896.
- Madam Marie Curie --- discovered radioactive substances radium, Uranium etc.
- Rutherford --- discovered nucleus, α -rays and β -rays.
- Chadwick --- discovered neutron.
- Maxwell --- discovered electromagnetic waves (invented by Hertz)

Radio Surgery

Stereotactic radiosurgery is a method of delivering high doses of ionizing radiation to small intracranial targets.

Methods are :

- **Gamma knife**
Focused γ -rays for small to medium sized brain metastases
- **Particle beam or cyclotrons**
Uses protons. Rarely used now a days
- **LINAC/ Linear accelerator**
Used for large tumours. Fractionated radiation may be used in multisessions.
- **Cyberknife**
Combines robotics and advanced image guidance to deliver

radiation to tumour along spinal cord/other critical location.

Characteristic appearances

- Spondylolysis - scotty dog wearing a collar app.
- Spondylolisthesis - Scotty dog with separated neck
- Scottish terrier sign - in oblique view

Soap bubble appearances

- Soap bubble appearance in abdominal X-ray --- Meconium ileus
- Soap bubble appearance in head CT --- Cryptococcal meningitis
- Soap bubble calcification in x-ray --- Osteoclastoma
- Soap bubble cerebral calcification in head CT --- Toxoplasmosis (Congenital)

→ *Puffed rice appearance on CT-Scan head is seen in --- neurocysticercosis*

- Ionizing radiation is produced by radioactive decay, nuclear fission and nuclear fusion, by extremely hot objects (the hot sun, e.g., produces ultraviolet), and by particle accelerators that may produce, e.g., fast electrons or protons or bremstrahlung or synchrotron radiation. In order for radiation to be ionizing, the particles must both have a high enough energy and interact with electrons. Photons interact strongly with charged particles, so photons of sufficiently high energy are ionizing. The energy at which this begins to happen is in the ultraviolet region; sunburn is one of the effects of this ionization.
- Charged particles such as electrons, positrons, and alpha particles also interact strongly with electrons. Neutrons, on the other hand, do not interact strongly with electrons, and so they cannot directly ionize atoms.
- They can interact with atomic nuclei, depending on the nucleus and their velocity, these reactions happen with fast neutrons and slow neutrons, depending on the situation. Neutron radiation often produces radioactive nuclei, which produce ionizing radiation when they decay.
- *Contrast nephropathy*: Contrast nephropathy is common with high osmolar contrast agents. It can be prevented by oral NAC with saline hydration prophylaxis. Preferred contrast agent should be of low osmolality.

SOME HIGH YIELD POINTS

- Investigation of choice in traumatic paraplegia - MRI
Intra-osseous skeletal tumours are best diagnosed by - MRI
- Investigation of choice for temporal bone injury - CT
- CT scan finding of adrenal incidentaloma:
Well circumscribed low density small round/ oval mass which accounts for 90% of incidentalomas.
- Lateral meningocele is c/by widened neural foramina -
- *In fibromuscular dysplasia* : string of beads appearance on angiography
- *Trethowan sign* : in Slipped capital femoral epiphysis
Sagging Rope sign : Perthes disease
Aneurysmal sign : Ant. Type TB - spine
- *Tree in bud sign* : Is a CT scan finding d/to airway plugging. Positive in tuberculosis and RSV infection.
- Trachea lies behind LA so in left atrial enlargement there is widening of tracheal bifurcation angle. Enlargement is best seen in penetrated chest x-ray PA view descending aorta is displaced to the left by LA enlargement (*Bedford's sign*) & in LA enlargement esophagus is displaced towards right & posteriorly
- Aortic knuckle shadow on CXR PA view is obliterated by consolidation of apico-posterior BPS of left upper lobe i.e. (posterior-basal part) of upper lobe.
- Most objective reliable sign of identifying pulmonary plethora in CXR is the diameter of descending right pulmonary artery >16 mm.
- Amount of air needed to produce death in air embolism → 200 ml
Echocardiography can detect pericardial effusion as little as → 15 ml
X-ray can detect pericardial effusion as little as → 250 ml
Minimum amount of ascitic fluid required to elicit puddle sign → 50 ml
Lateral view CXR can detect pleural effusion as little as → 50-100 ml .
- Effective radiation dose in radiological procedures

1. CT abdomen	-	10 mSv
2. CT chest	-	8 mSv
3. IVP	-	2.5 mSv
4. CT head	-	2 mSv
5. CT low dose protocol	-	1.5 mSv
6. MCU	-	1.2 mSv
7. CXR	-	0.02-0.04 mSv

- Tc 99 pertechnetate scan detects minimum of 0.1 mL blood.

SOME IMP. NEGATIVE POINTS

- On PA view X-ray chest cardiac silhouette is NOT increased in ---TOF
- NOT a Radiosensitizer substance ---Cyclophosphamide
- NOT a Radiosensitive tumour ---Osteosarcoma
- Miliary mottling is NOT seen in ---Staph.aureus pneumonia
- In chest X-ray PA view Rt heart border is NOT formed by ---Ascending aorta, RV
- NOT related to development of bladder cancer ---TB
- Skin tumours, which is NOT radiosensitive ---Malignant melanoma
- MCU is NOT indicated for ---Suspected renal tumours/mass
- Solitary pulmonary nodule is NOT seen in ---Neurofibromatosis / neurofibroma
- Air in biliary tract is NOT seen in ---Sclerosing cholangitis
- NOT true of adrenal incidentaloma ---Contrast is taken up early and washed out slowly
- Rib notching NOT occur in ---Waterson Cooley shunt
- B/L calcification of lung NOT occur in --- Klebsiella pneumonia
- Radioactive substance NOT used now a days --- Radium 226
- CT scan is least/NOT accurate in diagnosing--- 1 cm sized gall stone
- NOT an effect of radiation therapy on a child's brain --- IQ is affected significantly.

CLINICAL VEGNETTES

- CT scan of a patient with history of head injury shows a biconvex hyperdense lesion displacing the grey-white matter interface. The most likely diagnosis is:

[AIPGMEE 2003]

- A. Subdural hematoma
- B. Diffuse axonal injury
- C. Extradural hematoma
- D. Hemorrhagic contusion

(Ans. C. Extradural hematoma)

- An eight year old boy presents with back pain and mild

fever. His plain X-ray of the dorsolumbar spine reveals a solitary collapsed dorsal vertebra with preserved disc spaces. There was no associated soft tissue shadow. The most likely diagnosis is:

[AIPGMEE 2003]

- A. Ewing's sarcoma
- B. Tuberculosis
- C. Histiocytosis
- D. Metastasis

(Ans. C. Histiocytosis)

Histiocytosis is the m/c cause of single vertebra plana.

- A 15 year old boy was treated for retinoblastoma at the age of 1 year presented with pain and swelling around the knee, X-ray showed some typical appearance. Most likely diagnosis is

[AIIMS May, 2007]

- A. Ewing sarcoma
- B. Osteosarcoma
- C. Osteoid osteoma
- D. Chondrosarcoma

Ans.: Osteosarcoma

- A middle-aged female with epigastric pain since a month underwent CT abdomen, which revealed a mass lesion with grape like clusters in the head of pancreas with dilated pancreatic duct. Which of the following is the diagnosis?

- A. Solid papillary Pancreatic tumor
- B. Intraductal papillary mucinous neoplasm
- C. Mucinous neoplasm of pancreas
- D. Serous cystadenoma

(Ans. B. Intraductal papillary mucinous neoplasm)

- On ultrasound abdomen diffuse thickening of GB with hyperechoic shadow at neck and comet tail sign is seen in

[AIIMS Nov, 2008]

- A. Xanthogranulomatous cholecystitis
- B. Adenomyomatosis
- C. Adenomyomatous polyps
- D. Cholesterol crystals

(Ans.:B. Adenomyomatosis)

Adenomyomatosis

Adenomyomatosis appears on ultrasound as focal or diffuse thickening of the gallbladder wall. The gallbladder fundus is nearly always involved. *Rokitansky-Aschoff sinuses* are a characteristic morphologic feature. These are pockets of mucosa within the hypertrophied smooth muscle wall. These pockets commonly contain precipitated cholesterol crystals, which are very echogenic and produce comet-tail

artifacts. This benign condition has no malignant potential but may mimic gallbladder carcinoma on US studies.

Comet-tail artifact may be also seen in round atelectasis in asbestosis of lung. Abscess, Floating cholesterol crystals are seen as bright reflectors with short "comet-tail" artifacts. Air in bile has a similar appearance, Emphysematous cholecystitis

- A 40 year old man with head trauma and unconscious and multiple external injuries. CT-Brai – shows. No midline shift, No cerebral hematoma with multiple small hemorrhage with Basal cistern compression.

[AIIMS May'10]

- A. Diffuse axonal injury
- B. Multiple Infarcts
- C. Cerebral contusion
- D. Cerebral laceration

(Ans. A. Diffuse axonal injury)

- A middle-aged female is brought to hospital with h/o fever since 15 days with recent onset altered sensorium. CT brain shows enhancing basal exudates with meningeal enhancement. Which of the following is likely diagnosis?

- A. Herpes meningoencephalitis
- B. Tubercular meningitis
- C. Neurocysticercosis
- D. Pyogenic meningitis

(Ans. B. Tubercular meningitis)

Hx is s/o meningitis ?tubercular. CT brain in TBM is c/by meningeal enhancement and basal exudates.

- A young male with presenting complains of headache, vomiting, and ataxia is found to have a mass lesion with mural nodule which is located in right cerebellar hemisphere. What is the most probable diagnosis?

- A. Ependymoma
- B. Astrocytoma
- C. Hemangioblastoma
- D. Medulloblastoma

[Ans. : C. Hemangioblastoma]

Hemangioblastoma are cystic mass with a solid mural nodule found in cerebellum. A/w VHL syndrome and RCC.

- A 20 year old female presents with a mass in cavernous sinus + 6th CN palsy. In T2W MRI scan hyperintense shadow is present which shows homogenous contrast enhancement.

Most likely diagnosis is

[AIIMS Nov' 2010]

- A. Schwannoma
- B. Meningioma
- C. Astrocytoma
- D. Cavernous sinus hemangioma.

(Ans.: B. Meningioma)

- A young female presents with progressive lower limb weakness, spasticity, urinary hesitancy. MRI scan shows extra axial dural based mid dorsal enhancing lesion in thoracic region. Most likely diagnosis is

[AIIMS Nov' 2011]

- A. Dermoid cyst
- B. Meningioma
- C. Neuroepithelial cyst
- D. Intradural lipoma

(Ans.: B. Meningioma)

Intradural extramedullary tumour can produce symptoms of spastic paraparesis, bladder incontinence etc. Meningiomas are common intradural lesions. Most dural based (intradural) mass lesions are benign and slow growing. When spinal meningiomas grow into the epidural space compression symptoms. Enhancing dural tail sign can be seen.

If the lesions are multiple, neurofibromas are likely.

SOME IMP. NEGATIVE POINTS

CENTRAL NEURAXIAL BLOCKADE

- * Spinal cord extends from medulla oblongata to lower border of L_1 in adults and lower border of L_2 in infants & neonates)
- CSF volume is 130-140 ml ($\frac{1}{2}$ in cranium, $\frac{1}{2}$ in spinal canal); pressure is 10-12 cm H_2O or 8-12 mm Hg. produced @ 500 mL/d.

Subarachnoid Block (SAB)/ Spinal anaesthesia

- Spinal block /SAB /Intrathecal block is given in L_3 - L_4 interspace in adults (L_4 - L_5 in children)
- Produces **differential blockade**. i.e. autonomic level is 2 segment higher than sensory, which is 2 segment higher than motor blockade.
- Sequence of blockade: Autonomic \rightarrow sensory \rightarrow motor.
Order of sensitivity of nerve fibres to LA :
Autonomic preganglionic sympathetic (β) > Pain (C & A δ) > sensory > motor. β fibres are most sensitive to LA & spinal anaesthesia

- Drugs used are:

Ropivacaine 0.5% in dextrose
5% Xylocaine heavy

Levo-bupivacaine

0.5% Bupivacaine (sensocaine) heavy

- Structure pierced by spinal needle -
Skin \rightarrow s/c tissue \rightarrow supraspinous ligament \rightarrow interspinous lig. \rightarrow Ligamentum flavum \rightarrow dura \rightarrow arachnoid.
Drug is deposited b/w **arachnoid and pia**.
Loss of resistance is d/to piercing of ligamentum flavum.

- * MOA -Drug acts on spinal nerves and dorsal ganglia.

- Effect:

Tidal volume & ABG remain unchanged.

Only 2 things \downarrow : Maximum breathing capacity and active exhalation becoz of paralysis of i/c muscles.

CVS: Vasodilatation, venous pooling in legs, \downarrow BP & tachycardia.

- Factors affecting height or level of block.

- More volume, more height of block.

- Height of patient--in tall patient, more drug is required
- Obesity, ascites, pregnancy \uparrow es intra abdominal pressure so produces more height.
- Age ---elderly patient has reduced spinal space, so more height of block.
- Position of pt--- head down tilt, higher the level of block.

- Complications of SAB

- **Hypotension** - M/c c/c of SAB. Prophylactic measures are preloading with fluids, vasopressors. If hypotension develops, head low position to \uparrow venous return, O_2 , and vassopressors are useful. Ephedrine is DOC

- * Bradycardia - M/c arrhythmia

- Apnea
- Cardiac arrest
- N & V
- 6th cranial nerve is m/c nerve involved d/ to longest intracranial course.

Post Dural Puncture Headache (PDPH)

- Presents 12-24 hrs after spinal block.
- Usually *occipital* but c/b frontal
- \uparrow es on sitting & relieved on lying down
- Lasts for 2-3 days usually but may persist for 3 weeks
- **Predisposing factors** of PDPH: \uparrow es risk with
 1. Size: large bore > small bore needle (m/c factor)
 2. Type of needle: Dura cutting > dura separating
 3. No. of punctures: Multiple > single
 4. Age: **Young** > old
 5. Gender: Female > male

- * Cause - D/to CSF leakage through dural rent.

- Precautions: Use small size, dura separating needle, minimize the no. of attempts
- T/t: adequate hydration, prone or supine position, simple analgesics, Epidural blood patch, Oral or i/v caffeine, cosyntropin (\uparrow es CSF production) is newer drug for t/t of PDPH

- Absolute C/i of SAB

Relative C/i

- Patient refusal
- Raised ICT
- Coagulopathy or bleeding disorders
- Infection at site
- Shock
- Septicemia/ bacteremia

"PITKIN" / "GREUNE NEEDLE"

→ Quincke's needle is dura cutting spinal needle.

* Pitkin/Grene needle is spinal pencil tip needle which splits the dura → less incidence of PDPH

EPIDURAL BLOCK/ EPIDURAL ANESTHESIA

- Mainly used for postoperative analgesia, painless labour (labour analgesia), surgeries (abdominal, thoracic, neck)
- Commonly used epidural needle is **Tuohy's needle** (directional needle)
- Drugs used are : Lidocaine, bupivacaine, ropivacaine, mepivacaine, opioids.
LA act at nerve roots
Opioids act at substantia gelatinosa of dorsal horn cells.
- Given b/w dura and ligamentum flavum. Methods to locate epidural space (negative pressure test)
 - Hanging drop method (Guiretz sign)
 - Loss of resistance
- * Macintosh extradural space indicator
- * West Pal sign (Absence of knee jerk after epidural anaesthesia).
- Duran sign (Rapid injection in epidural space, causes ↑se in rate & depth of breathing). Seen in comatose pt.
- Ad/E of epidural opioid- nausea, vomiting, urinary retention, pruritus (itching), respiratory depression.
- C/c : patchy block, apnea, hypotension, total spinal, dural puncture, subdural block, intravascular injection.
- Advantages of epidural anaesthesia- less hypotension, no postspinal headache, level of block can be extended, any duration of surgery can be performed and can be used for post-op pain relief.

Labour analgesia

- **Epidural block** is one of the commonly used technique for labour analgesia.
- Ambulatory epidural labour analgesia or walking epidural is low dose CSE (combined spinal epidural) technique used for relieving pain during labour.

C/I of central neuraxial blockade (CNB).

CNB should be avoided if patient is on ---

1. Antiplatelet drugs (ticlopidine, clopidogrel, abciximab should be stopped 14d/7d/2d respectively before procedure)
2. Antifibrinolytic/ thrombolytic therapy

3. Oral anticoagulants : Warfarin should be stopped before CNB. A normal PT and INR should be documented.
4. Standard heparin in therapeutic dose ↑ PTT. Epidural catheter should be removed after stopping heparin.
5. In case of LMWH catheter should be removed at least 10 hr after the dose.

* [Aspirin/ NSAIDs, minidose s/c heparin are NOT a contraindication to epidural block or CNB.]

- Total spinal: Drug reaches upto medulla. so blocks CVS and respiration. Characterised by fixed dilated pupils, no respiratory effort, bradycardia. Patient becomes unconscious.
- High spinal: Causes hypotension with bradycardia. There is respiratory insufficiency but patient remains conscious.
- Differential blockade: Seen with **bupivacaine**. Low concentration produces sensory blockade while high concentration produces both sensory and motor blockade.
- When adrenalinic is given alongwith bupivacaine, it only ↑sensory blockade.
- * When adrenaline is given alongwith lignocaine it ↑sensory + motor blockade.

* Sedation and anaesthesia abolishes VER (visual evoked response), SSEP (somato-sensory evoked potential) are intermediately sensitive to anaesthetic agents and so MEP (motor evoked potential). But brainstem auditory evoked potential are least affected by anesthetic drugs.

ANAESTHETIC EQUIPMENTS

Oxygen Delivery Systems

- Non fixed performance device

Nasal cannula

O₂ concⁿ upto 44%

O₂ by Mask

O₂ concⁿ upto 60% by Merry Kettle mask.

- Fixed performance device

O₂ by Venturi mask

O₂ concⁿ upto 28- 60% Based on Bernoulli's theorem.
Used in patients with COPD.

- Room air provides 21% O₂.

Open System

* Schimmel Busch Mask was used for ether & chloroform

- Method : Open drop method. Disadvantages of this method were: open air pollution, can't regulate concentration, initial deep breathe or more drug can lead to unconsciousness.

Semi-open/Semi closed Systems (Mapelson Circuits)

- 6 systems are there:

Type	Also k/as	Best suited for	Feature/Advantage
A	Magill's circuit	Spontaneous ventilation	Fresh gas flow required to prevent rebreathing is equal to alveolar minute volume (MV = 70ml/kg/min) of patient. C/b used for both spont. + controlled ventilation. LACK's system is modification of 'A' with co-axial circuit (tube inside tube)
B	-	-	Obsolete
C	Water's to & Fro	-	Obsolete
D	Bain's co-axial system	Controlled ventilation	Inspiratory limb is inside the expiratory limb, Fresh gas flow required to prevent rebreathing is 1.6 MV
E	Ayre's T piece	Neonates	Inlet is near the face mask/ETT, used for weaning
F	Jackson Ree's	Pediatric ventilation	Modification of Ayer's T-piece /E used in children <6 yr or <20 kg

→ Fresh gas inlet is nearer to patient end in D, E, and F

→ Valveless circuits are E and F

→ Efficiency grading of Mapelson system

in spontaneous ventilation $A > D > F > E > C > B$

in controlled ventilation $D > F > E > B > C > A$ (A is least effective or not at all)

Closed Circuits/ Soda lime circuit

- Principle: Normal patient-
Breaths N_2O , O_2 and inhalational agents.
Expires N_2O , O_2 , inhalational agents and CO_2

If we pass whole expired gas through soda lime, it absorbs $CO_2 \rightarrow$ rest of gas can be re-used \rightarrow Requirement of fresh gas flow, more economical. All anesthetic agents react with soda lime to produce CO (Carbon mono oxide toxicity).

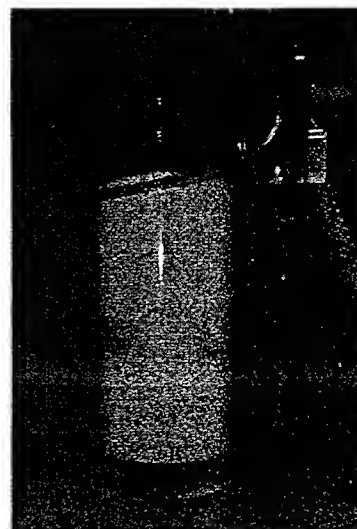
* Indicator added to soda lime changes the color of soda lime.

Indicators are -ethyl violet, mimoso-Z & phenophtalein.

- Mixture of 94% $Ca(OH)_2$ + 5% NaOH + 1% KOH
- Silicates are added to prevent powdering.
- Moisture 14-19% is also needed for efficient CO_2 absorption.
- It absorbs CO_2 and produces H_2O + heat, thus *humidifies and warms inspired gases*. 100 gm of soda lime can absorb 26 litre of CO_2 and temperature within the canister may \uparrow up to $60^\circ C$.
- Agents that should NOT be given with soda lime/closed circuit :
 - Trichloroethylene (trilene) because it generate phosgene which is neurotoxic.
 - Sevoflurane
 - Desflurane

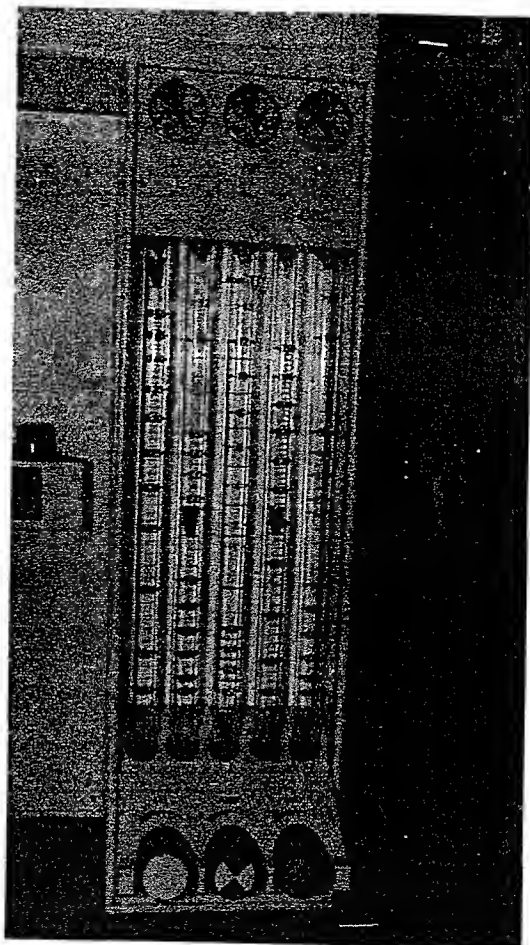
o Barylime is alternative to soda lime

	Sodalime	Barylime
Mesh size of granules	4-8	4-8
Composition	94% $Ca(OH)_2$ + 5% NaOH + 1% KOH	80% $Ca(OH)_2$ + 20% $Ba(OH)_2$
Absorption capacity	14-23 L CO_2 /100g	9-18 L CO_2 /100g
Moisture	14-19%	Nil
Hardness method	Silicates	Water crystallization
Advantage	-	Less caustic



Photograph : Soda Lime container

Flowmeter



Photograph : Flowmeter

- Flow tubes (Thorpe's tubes) are present inside the anaesthesia machine made up of pyrex glass.
- Each glass tube is calibrated a/c to gas it carries.
- Contain indicator for gas flow: Bobbin made up of aluminium.
- O₂ is downstream. O₂ flush can deliver 35-50 L/min of O₂.

ROTAMETER-

- * Variable orifice constant pressure flowmeter.
 - It has bobbin inside the calibrated thorpe tube, which indicates flow rate
- Inaccurate flow reading may be due to: Static electricity, dirt, non vertical position of tube, backpressure/backflow of gases, cracked flow tube.
- Position of O₂ is most downstream to all other gases. (To prevent hypoxia if tube breaks). In any event of leak O₂ is last gas to be added for safety.
- Systems used to prevent hypoxia:
 - low level O₂ pressure alarm

- Minimal O₂ /N₂O ratio controller device (hypoxic guard)
- O₂ concentration monitor & alarm
- * O₂ analyzer should have a low level alarm.
- * Mandatory minimal O₂ flow is 50-250 mL/min.

Boyle's anesthetic machine

- * "Continuous flow type of machine" to provide inhalation anesthesia, also used for artificial ventilation.
- It is normally equipped with 2 O₂ cylinder, 2 N₂O cylinder, 1-1 CO₂ & cyclopropane cylinder each.
- Cylinders are made up of Molybdenum steel to withstand high pressure.

Colour, Pressure & pin index of anesthetic gases

Gas	Physical form	Press. (psi)	Pin Index	Colour of cylinder
Air	Gas	1900	1-5	<u>Grey body / white shoulder</u>
O ₂	Gas	1900	2-5	<u>Black body/ white shoulder</u>
N ₂ O	Liquid	745	3-5	Blue
CO ₂	Liquid	838	1-6 (>7.5%), 2-6 (<7.5%)	Grey
Entonox (N ₂ O + O ₂)	Gas	1900	7	<u>Blue body/white shoulder</u>
Cyclopropane	Gas		3,6	Orange
Heliox, Helium	Gas		4,6 (>80.5%), 2,4 (<80.5%)	Brown

* Halothane --- colour of bottle is amber

- Halothane causes corrosion of metals & breathing circuits.
- Pin index safety system (PISS) is developed to discourage incorrect cylinder attachment. Used for small cylinders (<40 cubic feet).
- Diameter index safety system (DISS) is used to standardize connections b/w cylinders and flowmeters. (Pressure regulators). Each gas has specific attachments to prevent hook up of wrong gas. DISS number for-
N₂O 1040
O₂ 1240

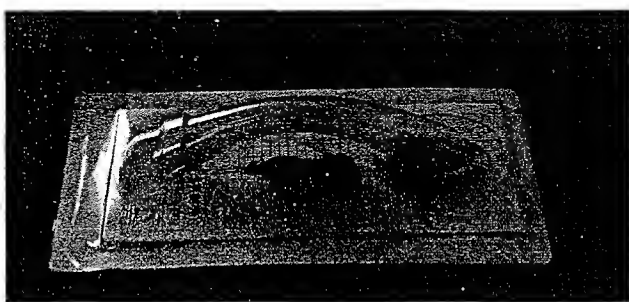
- **Cyclopropane:** Most inflammable & explosive agent. Liquid gas-Orange cylinder. Can cause cyclopropane shock.

Supraglottic airways

- LMA,
- Proseal-LMA (prevents risk of aspiration)
- SLIPA, Cobra
- I-gel

Laryngeal mask airway (LMA)

- Discovered by Dr. Archie Brain in 1980.
- Definitive supraglottic airway device.



- It is intermediate b/w face mask and ETT.
- * **Propofol** causes max^m depression of upper airway reflexes, DOC for LMA insertion.
- Uses:
 - Difficult airway
 - * For minor or day care surgery
- C/I: Full stomach, pregnancy, oropharyngeal mass, obesity
- Adv.: C/b used in CPR & in difficult airway becoz insertion is easy without laryngoscope, no m/s relaxation needed and c/b used by paramedics also.
- * For controlled ventilation Proseal LMA is used, while for spontaneous ventilation classical LMA is used.
- Disadvantage: Does not prevent aspiration of gastric contents. Selected acc/to weight of the patient

* Sealed LMA (Proseal LMA) prevents aspiration risk.

* Orotracheal or nasotracheal tubes are both supraglottic + infraglottic device.

ASSESMENT OF AIRWAY

1. Thyro-mental (b/w mentum & thyroid) distance should be >6.5 cm.

2. Sterno-mental distance should be >12.5 cm.
3. Adequate mouth opening : 3 finger breadth.
4. Mallam Patti grading

* Used for assesment of size of tongue for laryngoscopy.
(Inspection of oral cavity for intubation).

✓ Is for assesment of difficult airway during oro-tracheal/ nasotracheal intubation.

- 5 Grades :
 - 0 Visualise the tip of epiglottis
 - 1 Post. pharyngeal wall, faucial pillars, uvula, tip soft palate.
 - 2 faucial pillars, uvula without tip, soft palate.
 - 3 Only soft palate
 - 4 No soft palate.

* Intubation is difficult in Mallampatti grade 3 and 4.

Endo Tracheal Tubes (ETT)

- Murphy eye: In PVC tube small hole is present distal to cuff. If tube is blocked ventilation c/b continued with Murphy's eye.
- * Tracheal tube without Murphy eye is k/as Magill type tube.
- Cuff is high volume low pressure cuff. It lies in mid trachea (2-2.5 cm below the vocal cords)
- Cuff pressure should never exceed >30 cm of H₂O. Prefer 20 cm H₂O.
- * Cuffed ETT c/b used in long duration surgeries.

MONITORING

Minimum mandatory monitoring includes ECG, SPO₂, NIBP, ETCO₂, Temp ✓

Capnography

- It is monitoring of EtCO₂ (end tidal CO₂) and its waveform. Normally it is 35-45 mm Hg
- * Best tool for confirmation of the endotracheal tube placement. Detects early gaseous exchange.
- Notch in graph shows further requirement of m/s relaxant.
- Based on Mass spectroscopy, IR spectrometry (infrared rays are absorbed by CO₂), Raman spectrometry.
- Progressive zeroing in EtCO₂ is seen in ---
Esophageal intubation

- Sudden drop (upto 0) in EtCO_2 is seen in ---
Pulmonary venous air embolism
- Flat capnograph (straight line) is seen in ---
Intraoperative displacement of ETT, disconnection of ETT,
ventilation failure, cardiac arrest, esophageal intubation.
- Sudden rise in EtCO_2 is seen in ---
Malignant hyperthermia (upto 100 mmHg).
* Exhausted soda lime or defective valves of closed circuit.
- * In bronchospasm, capnograph shows increased resistance to airflow. Plateau prolonged.

Temperature Monitoring

- Site of Measurement-- axilla, rectal, oesophagus, UB, (right atrial temp monitoring is theoretically the most accurate), nasopharynx, tympanic membrane
- Ways of heat loss : radiation, conduction, convection, evaporation.
- * Usually rectal temperature is 2°C higher than core temp.
Axillary temperature is $1-2^\circ\text{C}$ lower than core temp.

Pulse Oximetry

- Works on principle of Beer-Lambert Law
- Sites of application of probe are: nail bed (fingers), toe, earlobe, nose, thenar and hypothenar eminence, sole of foot, wrist in neonates.
- * It measures O_2 saturation. It also monitors pulse rate and perfusion gradient.
- Inaccuracy is d/to ---
* Nail polish
* Methemoglobinemia (fixed SpO_2 of 85% is seen)
* Poor peripheral circulation (shock, hypotension)
* Carboxyhemoglobin
* Optical interference ambient light skin pigmentation

Invasive Monitoring

- Imp. methods are
 1. Intraarterial BP. (IBP)
 2. Central Venous Pressure (CVP)
 3. Pulmonary Artery Pressure (PAP)
- Used in
 - Extensive surgeries involving major fluid shift
 - * Cardiac patients
 - * Long duration of surgery
- 1. IBP: Direct measurement of arterial BP by cannulation of radial artery usually.

2. CVP:

- Measures RA pressure
- Used for infusion of drugs, fluids, TPN, aspiration of air in VAE
- * Normal CVP is $4-7 \text{ cm H}_2\text{O}$ ($3-12 \text{ mm Hg}$ is the range)
- Seldinger technique is used for catheterization of vein (guidewire technique for central venous access)
- * Veins commonly used - IJV, Subclavian, basilic/cephalic, femorals.

3. PAP (Pulmonary Artery Pressure)

- It requires Swan-Ganz pulmonary catheter (5 lumen)
- IJV is usually cannulated.
- Measures PAP, PCWP (indirect measurement of LA pressure or cardiac function), cardiac output, S_vO_2 (mixed central venous oxygen saturation), RVEF, CVP.
- Can also be used for air aspiration, infusion of drugs and fluids.

INTRA-OPERATIVE MONITORING, M/M

- Intraoperative awareness can be monitored/ prevented using Bispectral Index (B_{IS}). BIS c/b used to monitor depth of anaesthesia. BIS ranges from 100 to 0. BIS 100 means fully conscious. Value of BIS should be b/w 40-60 for adequate anaesthesia.
- Transesophageal echocardiography (TEE) is the monitoring tool which gives the best recognition of intraoperative myocardial ischemia.
- Neuromuscular (m/s relaxant) monitoring:
M/c nerve used is ulnar nerve (common peroneal c/b used also)
M/c m/s used is adductor pollicis s/by ulnar
* M/s to show earliest reversal orbicularis oculi (s/by facial n.).
- * Modes of monitoring are:
TOF (train of four), PTC (post tetanic count), tetanus, double burst stimulation.
- * Ionotrope of choice for intraoperative management of right heart failure due to pulmonary hypertension: Dobutamine and milrinone.
- Sitting position is avoided to prevent risk of air embolism during head and neck surgery.
- Induction & intubation
* Orbicularis oculi is monitored by TOF (train of four) ratio & single twitch stimulation.

- During maintenance profound block is monitored by PTC & TOF ratio using orbicularis oculi.
- During reversal phase :
 - TOF ratio is used to monitor adductor pollicis (TOF ratio of 0.3 for reversal administration and 0.9 for extubation).

GENERAL ANAESTHETICS

Inhalational agents

- No inhalational agent is good analgesic except N_2O (entonox). All inhalational agents have some m/s relaxant effect except N_2O .
- Main target of inhalational agents is brain.
- Classification of inhalational anaesthetics

Category	Example
Outdated	Ether, trilene, methoxyflurane, cyclopropane, chloroform
Gases	N_2O , Xenon
* Volatile	Halothane, enflurane, Iso, sevo, desflurane

MAC

- Potency of inhalational agent is determined by **Minimum Alveolar Concentration (MAC)** which is the concentration of agent, at which 50% of patients will not respond to the stimulus. So agent with minimum MAC will be most potent.

$$(MAC \propto \frac{1}{\text{Potency}})$$

Methoxyflurane is most potent while N_2O is minimum in potency.

- Factors which ↑ se MAC: Children, hyperthermia, anxiety, chronic alcohol ingestion.
- MAC ↓ es with old age, hypothermia, anaemia, pregnancy, hypoxia, coadministration with intravenous agent, N_2O and LA, acute alcohol ingestion.
- Factors that do not effect MAC are --- Sex (male or female), thyroid disease (e.g. hypo/hyper-thyroidism), hyponatremia.

MAC_{awake}

- MAC, at which 50% of patients will become awake.
= 0.3 MAC

B/G

- Blood Gas Partition Coefficient (B/G) determines speed of induction and recovery. Recovery will be faster with low B/G coefficient (e.g. N_2O , sevoflurane, desflurane).

Electrical (EEG) Activity of Inhalational Agents:

- Halothane - Typical biphasic pattern
- Isoflurane - Isoelectric EEG
- Des, sevoflurane - Burst suppression in high dose.
- N_2O - ↑ Both amplitude & frequency.
- Among IV agents BZD, etomidate produce typical biphasic pattern.
- Ketamine causes unusual activation (rhythmic high amplitude theta activity / β beta activity).
- Opioids cause Monophasic dose dependent depression on EEG.

- Factors affecting amplitude of EEG:

Factors	↑ by	↓ by
Inhalational agents	Subanaesthetic dose	Anaesthetic dose
* Hypoxia	Early ✓	Late
Barbiturate, etomidate	Small doses	Large doses
Others	N_2O , Ketamine, sensory hypercapnea	Opioids, propofol, Hypothermia

Halothane

- Potent volatile anesthetic (non inflammable, non-toxic)
- Sweet smelling agent. Causes smooth inhalational induction in children.
- Only alkane among fluorinated inhalational agents.
- Corrodes metals in vaporizers in the presence of moisture.
- Stored in amber colored bottles to prevent degradation.
- Vaporiser colour is amber/red.
- 0.01% thymol is added as preservative
- Undergoes maximum metabolism.
- Effects:
 - Bradycardia by delaying SA-AV nodal conduction.

Minimum
MAC

2. Hypotension by direct depression
3. Sensitize the myocardium to dysarrhythmic effect of catecholamines (adr). Adrenaline containing solutions should be avoided with halothane.
4. Abolishes hypoxic drive even at 0.1 MAC.
5. ↓ses IOP and BP, but ICT is ↑ed.

o Advantages:

1. It is a powerful bronchodilator, preferred in asthma
2. Uterine relaxant : DOC for manual removal of placenta. C/b used for internal version, tetanic uterine contraction.

3) DOC for HOCM **

o Disadvantages:

1. Malignant hyperthermia
 2. Significant relaxation of uterus can ↑ PPH.
 3. Does not provide any pain relief. Hyperventilate the pt prior to halothane administration becoz it blunts cerebral autoregulation.
 4. Causes shivering - Halothane shakes
↑ O₂ requirement by 500%. Best antidote for shivering is pethidine/tramadol.
 5. Halothane hepatitis (massive centrilobular necrosis) is a fatal condition in which mortality is 50%.
- o Can cause 5 'H' -hyperthermia, hepatitis, hypotension, hypercapnia, ↓HR (myocardial depression)
- * Should not be used within 3 month in the same pt.

TRILENE (Trichloroethylene)

- * It is a potent nerve poison. Vth & VIIth CN are m/c involved, but damage to 3, 4, 6, 10, 12 CN can occur.
- * Most potent analgesic agent because MAC is low 17%.
Used for trigeminal neuralgia & for labour analgesia
- o Not used now a days. 2-xenon 3-N₂O.
 - o Reaction with sodalime :- dichloroacetylene - neurotoxic-V, VII. Phosgene - pulmonary toxicity (ARDS)
 - o It is not used in closed circuit becoz it reacts with sodalime to form di-chloro acetylene (neurotoxic) and phosgene (pulmonary-toxic)
- $$C_2HCl_3 + NaOH \rightarrow C_2Cl_2 + NaCl + H_2O$$
- o At 125°C or in presence of O₂ as in cautery, it decomposes into phosgene (COCl₂) & HCl.
 - o Cardiostable. Does not depress myocardium/respiration.
 - o Disadvantage : Sensitizes heart to action of adrenaline (occasional dysrhythmias), tachypnea, addiction liability.

CHLOROFORM

- o 1st agent used for labour analgesia. Toxic agent.
- * Cardiotoxic agent. Can cause death due to ventricular fibrillation.
- * Highly emetic Causes post op nausea/vomiting.
- o Hepatotoxic. Causes profound hyperglycemia. Avoided in diabetics.

ENTONOX

- o 50:50 mixture of N₂O & O₂
- o Cylinder is blue coloured with white shoulder.
- * Use of Entonox include analgesia for wound dressing, chest physiotherapy, removal of chest drains, labour analgesia, & dental surgery.
- * It is good analgesic (d/to N₂O).

HELIUM

- o Isolated by Ramsay
- o Colorless, odorless, inert gas.
- * Heliox is a mixture of 79% helium + 21% O₂
- o Density is lighter than air, so useful in upper (NOT lower) airway obstruction. Also used to prevent N₂ narcosis.

XENON

- * Non-explosive, noble, colorless, odourless, inert gas.
- Non inflammable do not deplete ozone layer
- o Ideal but weak anaesthetic (No effect on CVS)
- o More potent than N₂O. MAC is 70% so can be given with 30% O₂.
- o Good analgesic.
- o B/G coefficient is 0.14 least of all. So fastest induction and fastest recovery
- * Not metabolized in body.
- * Good hemodynamic stability. Most cardiostable (Little change in BP & HR)
- * Can be used in a patient of MS with some liver compromise, used for radioactive study of CBF.
- o Least side effects non teratogenic.
- o Disadvantages : Expensive and not available easily.
Needs special equipment for delivery, bronchospasm.

NITROUS OXIDE (N₂O)

- o N₂O was named by Humphry Davy.
- o Synthesized by Priestley.
- o Also called laughing gas.

- * Lowest potency / efficacy (MAC 105%) poor anesthesia
 - o Good Analgesia
 - o **Fast induction d/to concentration effect**
 - o **Fast offset (recovery)**
 - o Non-inflammable, Non-irritating [**Safest anesthetic**].
 - o Colorless, odorless gas, supports combustion.
 - o Causes bone marrow depression → megaloblastic anaemia, peripheral neuropathy, pernicious anaemia.
- ✓ Has tendency to expand any air containing /close cavity, so **Contraindicated** in
 - Pneumothorax
 - Acute intestinal obstruction (volvulus)
 - Post.fossa Surgeries
 - Tympanoplasty
 - Lung cyst/bullae
 - Venous air embolism
- * Intraocular air bubble
- o Highly soluble. Diffusion hypoxia is seen in recovery phase
- * ↑ es uptake of other inhalational agents. Second gas effect is seen

ETHER

- o 1st public demonstraⁿ on 16th oct 1986 by W.T.G. Morton. So 16th october is celebrated as World anaesthesia day.
- * Pungent smelling (**unpleasant**)
- o High potency (MAC 1.9)
- * Agent with max^m skeletal muscle relaxation & good analgesia, so it is a complete anaesthetic agent.
- o Sa fest anaesthetic in untrained hands.
- ✓ Only inhalational agent that stimulates respiration.
- o Both induction and recovery are slow
- o Inflammable /highly explosive. Not to be used with cautery.
- * Does not sensitize the heart to the action of adrenaline (BP & respiration well maintained).
- o Highest incidence of nausea & vomiting among inhalational agent.
- o Only inhalational agent that preserves /maintains ciliary function (All other agents decrease ciliary activity)

METHOXYFLURANE

- o Most potent inhalational agent, as MAC is less. Not in use now a days. Most potent inhalational agent is M-F (MAC is 0.16%).
- o Slowest induction and recovery agent is M-F (B:G 15).
- o Non-inflammable, non-explosive. Good analgesic (like N₂O).

- o Most nephro-toxic agent is M-F (high output renal failure, highest fluoride toxicity). Metabolites are fluorides, which are excreted by kidney for up to 12 days. F⁻ is toxic to kidney & causes vasopressin resistant *high output renal failure*.
- * Advantage : No reaction with soda lime. Only inhalational agent that has boiling point more than water.
- * Disadvantage : Oxalate stones, hepatotoxic, most nephrotoxic.

Fluoride Nephrotoxicity

- o F⁻ is nephrotoxic. F⁻ is a byproduct of metabolism in liver and kidney.
- * F⁻ opposes ADH leading to polyuria. Maximum is seen with methoxyflurane :
Methoxy > Sevo >>> Iso > Des. Methoxyflurane results in potentially permanent renal injury. Less of a problem with modern anesthetics.
- * Among newer agents Fluoride content :
Sevo > des > en > iso > halothane.
However enflurane is more nephrotoxic than sevoflurane b/c of renal metabolism.

NEWER FLURANES

- * Sevoflurane & halothane are sweet smelling agent, so they are used for inhalational induction in children
- o Fluoride content /level is NOT or minimally affected by isoflurane, & desflurane.
- * Minimally/ NOT metabolized in the body → Desflurane
- o Inhalational agent of choice for :
 1. Neuro anaesthesia --- Isoflurane
 2. Cardiac anaesthesia --- Isoflurane
 3. Pediatric anaesthesia --- Sevoflurane
 4. Day care anaesthesia --- Desflurane
 5. Anaesthesia in Asthma --- Halothane

Enflurane

- o Epileptogenic inhalational agent.
- o Causes marked respiratory depression, myoclonus, seizures. Contraindicated in renal d/s & epilepsy.

Sevoflurane

- o Pleasant smell, non irritant and bronchodilatation makes it agent of choice for paediatric anaesthesia. **Induction agent of choice in children** b/c of sweet smell.
- o Less potent than isoflurane.
- o Sevoflurane reacts with soda lime used in anesthetic circuit to form "**compound A**" compound A is renal toxin.

Desflurane

- Fastest acting induction agent. **
- Agent that boils at room temperature (22.2°C). Melting / boiling point is very low 22.2°C (Special vaporizers needed i.e. Tec 6). B/G coefficient is lowest 0.45. Does not attenuate sympathetic stimulation. Pungent smell.
- * Desflurane's vaporizing chambers are heated to 39°C.
- Hepatic & renal blood flow are minimally depressed. So, Agent of choice for hepatic failure, renal failure. Agent of choice for geriatric (old) patients.
- Agent of choice for day care (fastest induction).

Isoflurane

- M/c used anaesthetic agent.
- IOP is best maintained but can cause coronary steal phenomena.
- Renal & hepatic function minimally affected
- Inhalational agent of choice for :
 - Cardiac anaesthesia / cardiac surgery (If LV function good),
 - For controlled hypotension
 - Neuro-anaesthesia / neurosurgery (maintains autoregulation & it causes min^m ↑se in ICT).^v
 Liver transplantation (only inhalational agent that maintains hepatic venous O₂ saturation).
- Fluoride metabolites are less.
- * Concentration effect with N₂O.
- * Sticker color is purple.

- Isoflurane causes "coronary steal phenomena".
- Thiopentone sodium causes "reverse coronary steal phenomena" or "Robbin-hood phenomena".
- Halothane blunts autoregulation.
- * If LV functions are poor- opioids are preferred induction agent of choice.
- Methoxyflurane is highly nephrotoxic. It causes high output renal failure.
- Isoflurane is anesthetic agent of choice in patient with renal / hepatic d/s and for cardiac or neurosurgery.
- * Fluoride level is NOT or minimally affected by isoflurane, & desflurane.
- Agents that should not be given with soda lime --- trielene. (trichlor ethylene), sevoflurane and desflurane
- * Most cardiostable volatile agent is isoflurane.

Volatile anaesthetics and effect on HBF (hepatic blood flow)

- * All volatile anaesthetic ↓ HBF
- * Halothane causes max^m ↓ HBF by ↓ ing cardiac output. Also causes halothane hepatitis **
- ✓ Ether and isoflurane preserve HBF

INTRAVENOUS GA AGENTSTHIOPENTONE

- Pale yellow coloured (d/to sulphur) powder.
- First used in 1934.
- Has very high pH (10.5-11), alkaline.
- Dose 3-5 mg/kg.
- Used in concentration of 2.5%. Concⁿ <2.5% causes awareness in patients.
- * Awareness assesment by monitor c/b done by BIS.
- Concⁿ >2.5% causes pain, necrosis.
- * Should be given in veins in outer aspect of the forearm.
- Never give in antecubital fossa. Chances of inadvertent intraarterial injection → Massive release of vasoconstrictors → pain, pallor/blanching, loss of distal pulse or even gangrene.
- It is treated by--leave the i/v cannula in situ → Flush NS then → Injection of vasodilator lignocaine/phentolamine, → Stellate ganglion block, brachial plexus block.
- * Thiopentone ↓es ICP and ↓cerebral metabolic O₂ demand by limiting CBF so cerebroprotective in nature. DOC for head injury pt.
- C/b used as an anticonvulsant (in status epilepticus)
- * C/i in acute intermittent porphyria & varigate porphyria. C/b safely given in PCT.
- * Ultrashort acting barbiturate becoz of redistribution away from brain is fast. Rapid onset GA with sedative, hypnotic & anti-convulsant property.

KETAMINE

- Produces dissociative anesthesia (thalamocortical limbic dissociation). Pt apparently remains conscious but unresponsive.
- Sleep occur within 5-10 minutes of i.m. injection or within 10-15 seconds of i.v. injection. Effect is d/to NMDA receptor blockade & lasts for 15 min [other NMDA receptor blockers are --- memantine & dextromethorphan].
- Profound analgesia. Only i.v. induction agent with analgesic effect.

- Rapidly acting parenteral anesthetic causing sedation, profound analgesia, cataplexy, some \uparrow in tone, mild CVS stimulation but only slight \downarrow of pharyngolaryngeal reflexes. It \uparrow es salivation (atropine or glycopyrrolate should be used with it).

- **Advantages:**

1. Maintains the upper airway reflexes so DOC for full stomach patient.
2. Anti dysrhythmia effect. (more in patient receiving TCA)
3. Minimal depression of respiration.
4. Potent bronchodilator. Refractory bronchospasm, can respond to ketamine. *Preferred in asthmatic.*
5. **Sympathetic stimulation** $\rightarrow \uparrow$ HR \uparrow BP (both SBP & DBP). DOC for **hypovolemic/shock** patients. Dose i/v 1-2mg/kg; i/m 5-10 mg/kg.

- **Dis-advantages:**

1. \uparrow BP : Avoided in IHD & hypertensive patients.
2. \uparrow ICT : Contraindicated in head injury and ICSOL patients.
3. \uparrow IOP : Contraindicated in glaucoma.
4. Potent bronchodilator. Refractory bronchospasm, can respond to ketamine. *Preferred in asthmatic.*
5. \uparrow CBF & \uparrow ICP can cause dreaming, hallucinations, delirium, non-purposeful limb movements & nystagmus. Sedatives like midaz/ diazepam should be co-administered. Unsuitable for neuroanaesthesia. Hallucinations caused by ketamine c/b \downarrow ed by midazolam.

- Particularly useful in **burn wound dressing**, skin debridement / graft

- * In debilitated patients in which catecholamines have depleted ketamine can cause myocardial depression.

- Ketamine \uparrow es all pressures i.e. ICP (or ICT), IOP (or IOT), BP (both SBP & DBP).

\rightarrow Ketamine causes --- \uparrow ICP

\rightarrow All inhalational agents --- \uparrow ICP (cerebral vasodilatation)

\rightarrow Thiopentone, midazolam, propofol cause --- \downarrow ICP

✓ Midazolam causes --- \downarrow HR, \downarrow BP & Anterograde amnesia

✓ Diazepam causes --- Retrograde amnesia

PROPOFOL

- Rapid onset (within 40 seconds of administration).
- DOC for *day care surgery*.
- * Propofol is an IV sedative / hypnotic used in induction / maintenance of anesthesia in day care surgery.
- Max^m depression of upper airway reflexes, DOC for LMA insertion.
- ✓ Poor analgesia (supplementation with narcotic is required for analgesia).
- * Causes dose dependent myocardial suppression, hypotension with bradycardia (\downarrow BP, \downarrow ICP). Used with great caution in cardiac patient. [Remember: pancuronium causes hypertension + tachy^y]
- Reduces nausea and vomiting.
- Propofol is made up of soyabean oil, glycerol & egg lecithin. Open vial of propofol is a good culture media for bacterial growth. Risk of sepsis if propofol is used after 6 hrs.
- Milky white in colour. Injection is very painful bec/ of oil/ lipid emulsion, so xylocaine is either mixed or administered before propofol injection.

ETOMIDATE

- It is a sedative hypnotic but not an analgesic
- Most cardiostable agent (Do not \uparrow or \downarrow HR) so agent of choice for aneurysm surgery & pt. with cardiac ds.
- * Causes maximum post op nausea, vomiting.
- ✓ Myoclonus and suppression of adrenal cortex, so \downarrow es cortisol level. Used for emergency purpose only
- * Contraindicated in patient of porphyria and adrenal insufficiency.

FENTANYL

- * More potent analgesic than morphine.
- Rapid onset & rapid recovery so used for day care surgery.
- Rapid injection of high doses produces significant m/s rigidity/ chest tightness (**Wooden chest syndrome**)
- Can be given in hepatic & renal ds pt.

REMIFENTANIL

- Ultra short acting opioid
- ✓ Used in TIVA along with propofol
- Used as infusion d/to context sensitive half life of 3-5 min.

LOCAL ANAESTHETICS

LIDOCAINE (Lignocaine, xylocaine)

- * Xylocaine 2% is used in dose of 3-5 mg / kg
- o Xylocaine 2% with adrenaline is used in a dose of 5-7 mg/kg.
- o Xylocaine with adrenaline should **not** be used for ring block, penile block .
- o **Xylocard** (Xylocaine without preservative) is the only preparation of xylocaine used i.v.
- o Uses - spinal block, epidural block, regional nerve block, ventricular fibrillation, as local infiltration, to blunt hemodynamic response to intubation
- o S/E in high dose convulsion, hypotension, cardiac arrest, resp. depression
- o Xylocaine is neither vasoconstrictor nor vasodilator (very little vasodilatation activity may be seen)
- o M/A---By blocking Na⁺ channel.

BUPIVACAINE

- o More cardiotoxic than lignocaine.
- o Long acting drug. Effect lasts for 6 hrs.
- o Hyperbaric solution of B~ is injected as a single shot into CSF to produce intense (usually within 5min) blockade (spinal/ intra-thecal anesthesia).
- o Should **not** be used in Bier's block (because of its cardiotoxic potential).
- o **Cardiotoxic.**
- o Used for skin infiltration, epidural, spinal regional nerve block
- o Less placental transfer. Fetomaternal ratio is 0.32 so used in labour/ obstetric analgesia.

Topical Anaesthesia

Used on skin, urethral mucosa, nasal mucosa, cornea etc.

Agents used are :-

- o *Amethocaine (Tetracaine)*
Well absorbed by mucosa
- o *Cocaine*
Only LA which is **vasoconstrictor**. Cocaine + adrenaline co-administration is contra- indicated. Only indication of cocaine is topical anaesthesia of eye.
- * EMLA cream (Prilox) is Eutectic mixture of lignocaine + prilocaine (2.5%/2.5%). Used in children before venepuncture (to decrease needle phobia) LP.
- o Lignocaine jelly (LOX jelly) /lozenges are used sometimes

to relieve sticking sensation in throat.

- * LA which anesthetize intact skin - Amethocaine, Prilocaine, Eutectic Lignocaine 5% and prilocaine 5% EMLA cream (Topically applied for venipuncture, needle procedure and LP).

- * Methemoglobinemia is c/by prilocaine and benzocaine mainly.

* Cocaine was the first LA used clinically while procaine was the first synthetic compound.

→ All LA are vasodilator except cocaine (vasoconstrictor)

→ Shortest acting LA is chlorprocaine while longest acting LA is Dibucaine

→ S/E in high dose convulsion, hypotension, cardiac arrest, resp. depression,

✓ Ester linked local anesthetic cause more allergic reactions (d/to PABA)

✓ Ester linked local anesthetic are metabolized by cholinesterases while amide linked LA are metabolized in liver

Addition of sodabicarb to LA

- * ↑ es the un-dissociated/ un-ionic form.
- o Block becomes faster, longer & of better quality.
- o **Cocaine** : Causes local vasoconstriction
- * **Prilocaine** : Does not causes vasodilatation, hence used in Bier's block
- o **Lignocaine** : No effect on blood v/s, Eutectic mixture (EMLA cream) is used for venipuncture.

MUSCLE RELAXANT

Classification

	Action	Example
o Non-depolarising agent (NDMR) (Competitive)	Long acting	d-TC Pancuronium Doxacurium Pipcurium
	Intermediate	Vecuronium Atracurium Rocuronium
	Short acting	Mivacurium, Rapacuronium
o Depolarising agents (Non-competitive)	Shortest acting	Sch Decamethonium

Skeletal M/s Relaxants : Summary

M/s Relaxant	Advantages & Sp/f	Metabolised by	Histamine release	Contraindications & Disadvantages
• Gallamine	Vagal blockade	Renal (100%)		Renal failure, MG, pregnancy Crosses placenta, less potent
• d-TC (Tubocurane)	✓ MR of choice in obstetrics, Ganglionic blockade, Good for arterial/vascular Sx		+++	Myasthenia gravis
• Sch (Scoline)	Shortest acting MR, MR with fastest onset, Vagal & ganglion stimulation	Pseudocholinesterase	+	Avoided in Spinal cord injury, burns, cerebral palsy, 48h-9mo after injury C/ind in AIP, DMD, malignant hyperthermia
• Pancuronium	✓ Preferred in hypovolemic shock, longest acting	Liver, renal	- (virtually nil)	CVS instability, max ^m vagal block (Causes hypertension with tachy), renal failure
• Vecuronium	Most cardiostable	Liver		
• Mivacurium	✓ Ultra short acting NDMR (duration 12-18 min), So given by continuous infusion	Pseudocholinesterase	+	Slow onset
• Atracurium	Safe in renal/liver d/s	Hoffman's elimination (70%) Ester hydrolysis (30%) → Laudanosine		Seizures
• Cis-atracurium	4 times more potent than Atrac, Less histamine release	100% Hoffman's elimination, Laudanosine levels are much lower	-	
✱ Rocuronium	NDMR with fastest onset	By liver		✓ Least potent NDMR, causes pain on i/v injection

Depolarising Vs Non-depolarising Block

Characteristics	Depolarising (Phase I) block	Non-Depolarising (Phase II) block
1. Tetanic stimulation	No fade	Fade
2. Train of four stimulation	No fade	Fade
4. Post tetanic facilitation	None	+

- Fading is seen with NDMR in a 'train of four' ratio.
- Post tetanic potentiation is seen in NDMR.
- Neostigmine antagonises competitive blockade.

Sch (Suxamethonium/ scoline)

- Depolarising MR. (Acts by persistent depolarisation)
- Shortest acting MR
- Most rapid onset of action & shortest duration of action.
Used for Rapid Sequence induction
Onset of action 10-30 sec, duration 3-5 minutes

- Metabolised by plasma cholinesterase by rapid hydrolysis. (Do not require antagonists for reversal of blockade).
- In pt with pseudocholinesterase deficiency duration of action is prolonged, which c/b managed by IPPV, FFP's, neostigmine.
- Dose 1-1.5 mg/kg
- Normally causes **phase I block** (causes muscle fasciculations and then relaxation) but repeated & large dose (>5mg/kg) can cause phase II block and features of NDMR like fading & reversal with neostigmine.
- S/E
 - Postoperative **muscle soreness / myalgia**
 - Bradycardia common in children esp after 2nd dose,
 - Cardiac arrest (Sch acts on SA node)
 - Hyperkalemia (seen in burns < 3 month, tetanus, S.C. injury, LMND, CP, Duchenne muscle dystrophy)
 - Prolonged apnea
 - It ↑ IOP, ICP and intragastric pressure

- ✓ Does not cross placental barrier, so good for operative obstetrics & LSCS
- * Can be given in myasthenia gravis but is avoided in Duchenne muscle dystrophy
- Causes hyperkalemia and leads to cardiac dysarrhythmia and cardiac arrest in patient with burn, massive trauma, neurological d/s, tetanus, myopathies, severe intra-abdominal sepsis.

MIVACURIUM

Shortest acting NDMR. Does not need reversal as rapidly metabolised by plasma pseudocholinesterases.

ATRACURIUM

- Short acting NDMR
- Safe in-patient with renal or hepatic disease.
- **Hoffman degradation** (inactivation of drug in body fluids by spontaneous molecular rearrangements and its spontaneous elimination at normal body temperature and pH) is seen. Also metabolized by ester hydrolysis.
- Its metabolites are : Laudanosine (epileptogenic property) and acrylate.
- Causes histamine release, anaphylaxis, seizures (d/to laudanosine).

ROCURONIUM

- * Intermediate duration, fast acting NDMR with onset of action within 90-120 seconds in a dose of 0.5 to 0.6 mg/kg and 60 - 90 seconds in a dose of 0.9 to 1.2 mg/kg.
- Action lasts longer. Provides rapid intubation conditions.
- Used for RSI (rapid sequence intubation) where Sch is contraindicated. Can be used i/m!
- Rocuronium has replaced vecuronium in countries where it is available.

RAPACURONIUM

- * New steroidal NDMR with rapid onset of action.
- Least potent.
- Least CVS ad/E, **short duration of action.**
- * Causes histamine release and severe bronchospasm so therefore withdrawn from market.

GALLAMINE

- Least potent MR but potent vagolytic Not used now a days.
- 80% excreted by kidney.
- **Contraindicated in pregnancy, renal disease.**
- Patient suffering from MG are most sensitive to gallamine (competitive blocker of Ach → more weakness).

→ Shortest & fastest acting MR (Overall) --- Sch (Scoline)

→ Shortest acting NDMR (CNMB) --- Mivacurium

→ Fastest acting NDMR --- Rocuronium

→ Longest acting NDMR --- Pancuronium

→ MR of choice to ↓ BP in arterial surgery --- d-TC

* MR of choice to maintain BP in arterial surgery

--- Pancuronium

(CNMB = Competitive N_M blocker)

* M/c used SMR in routine surgery

--- Vecuronium

* Most potent SMR

--- Doxacurium

→ Least potent SMR

--- Sch

→ Least potent NDSMR

--- Rocuronium

(SMR = Skeletal Muscle Relaxant)

D-TUBOCURARINE (d-TC)

- Not used now a days.
- ↓es BP.
- * Induces histamine release & promote ganglionic blockade.
- It requires reversal with neostigmine
- It does not cross placental barrier, so M/R of choice in obstetric patient.

MALIGNANT HYPERTHERMIA

- Life-threatening genetic abnormality of skeletal muscles char/by sympathetic stimulation tachycardia, tachypnea, ↑BMR, hyperkalemia, muscle rigidity, hypertension, DIC, and fever. Seen in children of m/s dystrophy.
- Masseter m/s rigidity is the earliest definitive sign and hypercapnia is the earliest biochemical change

- *Triggering anesthetics* *Safe anesthetics in M-*
 1. Fluorinated anesthetics, vapors 1. N_2O
(Halothane, isoflurane, Methoxyflurane)
 2. Propofol, Ketamine, opioids, Barbiturates, sodium pentothal, BZD
 2. Depolarizing blocker 3. NDMR (d-TC)
(S-ch, Decamethonium)
 3. Ether, some neuroleptics 4. LA
[mnemonic: FHS Eventually trigger MH]
- Sch causes MH in immediate post op period (within hours).
- T/t :
Cooling of body, hyperventilation with O_2 ,
Specific antidote : **Dantrolene - sodium** (Bromocriptine is also useful). Dantrolene sodium interferes with the release of Ca^{++} ions from SR^f (sarcoplasmic reticulum) → Inhibit ryanodine receptors → Decrease intracellular Ca^{++}

PEDIATRIC ANESTHESIA

- Best inhalational (volatile) induction agent – sevoflurane
- * Narrowest part of larynx is cricoid – to avoid pressure necrosis of it, uncuffed tube is used in neonates and small children.
- * Larynx is anterior and high up so straight blade (Miller's type) laryngoscope is used
- *Induction agent of choice* :
Method of choice for induction is intravenous if i.v. access is already present). otherwise inhalational.
- Best inhalational agent --- Sevoflurane in N_2O & O_2
- I/v rapid acting --- Thiopentone, propofol (>2 yr)
f/b NDMR
- Best i/m agent --- Ketamine
- Inhalational induction agent of choice is sevoflurane.
- * Circuits used for pediatric pt. upto 20 kg Jackson Ree's modification of Ayre's T piece (JRM Circuit) or Mapelson F
- Body surface area is larger so prone for hypothermia (to prevent hypothermia, non shivering thermogenesis occur)
- ✓ Caudal block is m/c used for postoperative pain relief in children in lower abdominal, perineal, or LL surgeries.
- Isolyte P is maintenance i.v. fluid of choice in pediatric age

patient upto 5 years.

- Pediatric age group patients with congenital myopathies are susceptible for
 1. Marked hyperkalemia --- Avoid scoline
 2. Malignant hyperthermia --- Avoid triggering agents (Sch, neuroleptics, volatile agents e.g. ether & fluranes)
 3. Occulocardiac reflex --- D/t traction on extraocular m/s during surgery
it is trigeminal reflex, leads to bradycardia and sinus arrest
Treated by inj atropine, deepening the plane of anaesthesia, stop scoline.
- * In male children < 2yrs avoid scoline d/to risk of dangerous hyperkalemia in an undiagnosed case of DMD.
- A child with exstrophy of bladder + renal failure was posted for repair, MR of choice is --- Atracurium
- * A child with Duchene MD was posted for surgery, anesthetic agent of choice is --- Propofol

OBSTETRICS ANESTHESIA

- Regional Anesthesia is preferred over GA in pregnant patient b/c of risk of aspiration and difficult airway d/ to edema.
- Prolonged labour can lead to carpopedal spasm d/to hyperventilation → alkalotic/hypocalcemic tetany.
- Epidural anesthesia is preferred for labour analgesia. Drug useful in painless labour (epidural analgesia) is bupivacaine. **Bupivacaine** is the m/c LA used b/c of low fetomaternal ratio, and it produces **differential blockade** i.e. sensory blockade at low dose while motor blockade at higher doses.
- *Indication of GA*
 - Manual removal of placenta
 - Fetal distress during second stage
 - Tetanic uterine contraction
- * Thiopentone (and propofol also) is the induction agent of choice
- *Mendelson's syndrome*:
Aspiration of gastric content during anesthesia. Risk factors

include pH < 7.35, gastric volume > 25 ml. It c/b prevented by

- * Aspiration prophylaxis with sodium citrate, H₂ blockers
- * Rapid sequence Induction i.e. preoxygenation, Sellick's manoeuvre, i.v. Induction / Sch intubation
- o Supine Hypotension syndrome;
Occurs d/to compression of IVC by gravid uterus and is seen in last trimester. M/m includes lying in left lateral position or displacement of gravid uterus by keeping wedge under right lumbar region to prevent this complication.
- * Drugs used for obstetric labour analgesia --- Entonox, pethidine
- * Drug useful in painless labour --- Bupivacaine
- * Pudendal block is useful in episiotomy.

ANESTHESIA IN SPECIAL SITUATIONS

Anaesthesia in Geriatric pt/ Elderly

- o Elderly persons require less dose of anaesthetic agent d/to age related physiological changes
- * Induction agent of choice : Etomidate, thiopentone.
- o Inhalational agent of choice for maintenance of anaesthesia: Isoflurane/desflurane.
- o Methoxyflurane is nephrotoxic, so should not be used.
- * More prone for post-operative delirium

Anaesthesia in a patient of epilepsy

- o Enflurane : Causes GTCS. So contra-indicated in seizure disorder.
- o Sevoflurane : Can rarely cause convulsions.
- o Atracurium : Its metabolite laudanosine can cause convulsions. avoided in epilepsy.
- o Ketamine : Increases ICP → Convulsions.
- * Rocuronium : No effect on ICP → Safe

Anaesthesia in Renal Failure patient

- o We should avoid volatile agents like enflurane, sevoflurane, methoxyflurane (Prefer--- Isoflurane, desflurane, halothane)
- * M/R to be avoided are --- Gallamine, & pancuronium (prefer--- Atracurium, vecuronium)
- o Pethidine should be avoided in renal failure.

Anaesthesia in Asthmatic patient

Drugs safe in Asthma

- o Best inducing agent -- Ketamine, propofol
- * Best GA in status-- Ketamine [relieves asthmaticus bronchospasm]
- ✓ Best skeletal MR -- Pancuronium, vecuronium
- o Other GA safe in asthma -- Halothane (it inhibits cough, pharyngeal & laryngeal reflexes, produces bronchodilatation)
- ✓ N.B. Thiopentone sodium is contra-indicated in asthma as it precipitates bronchospasm]
- Muscle relaxant safe in renal failure pt--- Atracurium, Vecuronium
- Safe in hepatic failure pt--- Atracurium
- ✓ Suitable anesthetic agents in chronic alcoholism--- Isoflurane & Sevoflurane

Anaesthesia for cardiovascular surgery

- o Induction agent of choice for R → L shunt (Cyanotic HD) --- Ketamine
(Because ketamine ↑es systemic vascular resistance but does not ↑se pulmonary vascular resistance, and thus does not ↑ R → L shunt)
- * Induction in a pediatric patient with L → R shunt (Acyanotic HD) is done by --- Sevoflurane
Or any other i.v. induction agent except ketamine
- * Anaesthesia is maintained in cardiac patient with --- O₂ + N₂O + opioids.

Anesthetic consideration in special situations

- o A patient with SCD (sickle cell trait) posted for surgery in left arm---
Tomiquet should be avoided as it can produce vasoconstriction and stasis of blood leading to hypoxia. IVRA (Beir's block) should be avoided
- o A patient with mitral stenosis is posted for surgery. Hc is having some liver compromise---
Preferred inhalational agent for him is Xenon and sevo.
- o Anesthesia in burn patient
Anectine safe in 1st 24 hrs. Ketamine for dressing changes & escharotomies.

Anesthetic (Induction) agents of choice for

Condition	DOC
• Day care	Propofol
• Epilepsy	Thiopentone
• Neurosurgery	Isoflurane
• ECT (Electro convulsive therapy)	Methohexitone
* <u>Bronchial asthma</u> <u>COPD</u>	<u>Ketamine (i/v),</u> <u>Halothane (inhalational)</u>
• IHD (Ischemic heart d/s)	Etomidate
✓ Cardiac surgery →	Isoflurane
• CHD : Lt to right shunt	Isoflurane
• CHD : Rt to left shunt	Ketamine
• CHF	Ketamine
• Shock	Ketamine
* I/v agent for induction in children	Ketamine
• Inhalational agent for induction in children	
✓ For induction in <u>elderly</u>	<u>Etomidate/thiopentone</u>

✓ ELDERLY
→
✓ ETOMIDATE
✓ THIO PENTONE

✓ For neurosurgery preferred induction agent is isoflurane with thio/propo/eto + hyperventilation to maintain PaCO_2 b/w 25-30 mmHg.

✓ For CAD (IHD) surgery barbiturates, BZD's, propo/eto are equally safe.

Drugs for day care surgery (OPD Anesthesia)

- Inducing agent of choice -- Propofol
 - Volatile anesthetic of choice -- Isoflurane (now-a-days sevoflurane, Desflurane)
 - Analgesic -- Alfentanyl, Remifentanyl, Fentanyl
 - Muscle relaxant -- Mivacurium, atracurium
- Remember that alfentanyl, remifentanyl, mivacurium although are theoretically best agents but are not available in India

Selection criteria for Day care surgery

- Patient should be managed with oral analgesics.
- Vitals stable.
- Responsible adult accompanying.
- ASA grade I - III.
- No hematoma.
- Walk easily.

Drugs before surgery / Drugs in PAC

Drug	Advice
• Antipsychotics	
✓ Warfarin	<u>Discontinue 4-5 days before</u>
- Heparin	Delay s/c heparin till block
• Antipsychotics	To be continued
• Lithium	To be continued Potentiates DMR & NDMR
• TCA	To be continued ↑ sensitivity to CA's
• SSRI	To be continued Check s. electrolytes, hyponatremia
• <u>MAOI</u>	<u>Omit 24 h prior to Sx</u>
- Tranylcypromine,	Stop 2 wks prior
- Phencyclidine,	
- Isocarbazide,	
- Selegiline (<10 mg/d)	
✓ <u>Combined pills (OCPs)</u>	<u>Stop 4 wks prior</u>
• HRT	Stop 6 wks prior to major Sx
• POP	C/b continued
• CCBs, β blocker, nitrates	To be continued
✓ ACEi	<u>To be stopped 24 h prior to Sx</u>
• Diuretics	To be continued
• Antihypertensive	To be continued
• For induction in elderly	Etomidate/thiopentone

ASA Grading for risk of anaesthesia

- Grade I - Patient with no systemic d/s.
- Grade II - Mild systemic d/s (well controlled)
- Grade III - Moderate systemic d/s with functional limitation.
- Grade IV - Severe systemic d/s with constant threat to life.
- Grade V - Moribund patient which is going to die within 24 hr with or without surgery.
- Grade VI - Brain dead patient for organ donation.

Stages of anaesthesia

- Described on ether by Goodell.
- I - Stage of analgesia
- II - excitement (pupils dilated)
- III - Surgical anaesthesia. Has 4 planes
 - III, plane III : Laryngeal paralysis
 - III, plane IV : fully dilated pupils
- IV - Coma
- Intubation c/b done in stage III, plane III

DIFFERENT BLOCKS

IVRA /Bier's block (I.V. Regional Anaesthesia)

- ✓ Large amount of LA is injected in veins after using tourniquet.
- Lignocaine without adrenaline is the DOC. Prilocaine (0.5%) is also safe.
- Used in both UL & LL i.e. forearms and hands (e.g. reduction of colles #)
- Bupivacaine is contraindicated for IVRA bec/ of its high cardiotoxicity which may occur after release of tourniquet.
- Contraindications for IVRA: Raynaud's, SCD, scleroderma.
- Tourniquet time for UL is 45-60 minutes and for LL is 60-90 minutes

TIVA (Total Intravenous Anaesthesia)

- Used for day care surgery, neurosurgery.
- Combination of propofol and Ramifentanyl is used.
- Only inhalational which c/b used: O_2 , NO , N_2O
- Advantages over inhalational induction & maintenance:
 - * Smooth induction with minimal coughing and hiccoughs.
 - Easy to control depth of anaesthesia.
- * Less PONV
- * ↓ CBF & ↓ cerebral metabolic rate are favorable for neurosurgery.

Caudal block(Epidural sacral block)

- It is commonly used regional anaesthetic technique in children for perioperative and postoperative pain relief.
- Mainly used in children for perineal surgeries, genitourinary surgeries.

Brachial Plexus Block

There are many approaches of brachial plexus blocks

* Supraclavicular block :

M/c used method of brachial plexus block.

◦ Axillary block , Interscalenae block :

Intraclavicular approach for upper arm surgeries interscalenae approach is preferred.

◦ Coeliac plexus block

Used for lumbar sympathetic chain. Decreases pain in pancreatic cancer, stomach cancer. Can cause hypotension.

Retrobulbar Anaesthesia

- LA is injected behind the eye into the cone formed by EOM (extraocular muscles).
- * Effectively blocks all EOM within seconds except superior oblique.
- ✓ Affects the ciliary ganglion (Results in pupillary dilatation) **

PAIN MANAGEMENT

- If a patient undergoing thoracotomy complains of severe pain, he should be best managed by IV fentanyl ✓
- * Oral morphine or oral brufen are not used in t/t of severe pain in immediate postop period in a thoracotomy patient.
- * Systemic opioids alone are effective in controlling background pain.
- Pain scale----
- * VAS (Visual analog scale) in adults.
- FACES scale, and CHEPOES scale (Children's Hospital of Eastern Ontario Pain Scale) in children.
- * Mc gill questionnaires used for pain in adults.

AD/E OF ANAESTHETIC & RELATED DRUGS

◦ Methemoglobinemia is seen with :

- Prilocaine
- Lignocaine
- Benzocaine
- N_2O , Nitrites

* Sulfonamides, phenacetin

- Muscle pain / soreness --- by Sch.
- ✓ Muscle spasm (intra-operative) --- Fentanyl
- ✓ Muscle Tone --- Ketamine
- * Opioids (fentanyl, sufentanyl, alfentanyl) induce → M/s rigidity or Chest wall rigidity.

- * ↑ BP - Ketamine, pancuronium, pentazocine.
- o (i) ↑ ICT - Ketamine, Halothane, Sch.
- (ii) ↓ ICT - Isoflurane, Propofol, etomidate, lidocaine, cyclopropane, BZD (midaz)
- o (ii) ↑ IOT - Ketamine (transient), Sch, N₂O, etomidate, thiopentone.
- (ii) ↓ IOT - Halothane, morphine.
- o (i) Bronchospasmodic - Ether, N₂O, thiopentone.
- (i) Bronchodilator - Ketamine, halothane, promethazine, morphine, dTC.
- o Intra-arterial injection of thiopentone causes → intense pain, inflammation & necrosis
- Intra-venous injection of thiopentone → No pain
- Intra-venous injection of propofol → Pain
- * Propofol supports → Growth of bacteria.
- o Ketamine produces → Dissociative anaesthesia.
- o In MG - Sensitivity of Gallamine and d-TC is increased while that of Sch. is decreased.
- CVS Ad/E - Halothane > Enflurane > Isoflurane
- * Ether, Iso-, Sevo & Enflurane does not sensitize the heart to the action of catecholamines /Adr.
- o Drugs which sensitize the heart to the arrhythmogenic action of catecholamines /Adr are---
Halothane, methoxyflurane, trichlorethylene, Cyclopropane, chloroform so these drugs are not used now a days.

POINTS OF SPECIAL MENTION

- * Plasma cholinesterases degrades :
 - Sch.
 - Mivacurium, Cis-atracurium
 - Propanidid
 - Esmolol
- o Etomidate and propofol have no active metabolite.
Ketamine produces Nor ketamine, while midazolam produces hydroxymidazolam.
- * Esophageal carcinoma require one lung ventilation & deflation of another lung. Robertshaw and Karland tube is used.
- * M/c cause of hypoxia with one lung ventilation - malpositioning of tube.
- o Left lobe is the best region for auscultation in ETT intubation.
- * Flexometallic tube: Used for spine, head and neck surgery and for surgery in prone.

ZEOLITE
→ Al(OH)₃ to absorb N₂

- o Coles tube: Used in children.
- * Polard's tube: Used for microlaryngeal surgery.
- * Zeolite is aluminium hydroxide to absorb nitrogen. Can provide 95% oxygen. Electronically powered.
- * Muscle relaxant
 - Safe in renal failure - Atracurium, Vecuronium
 - Safe in liver failure - Atracurium
- * Procaine & Bupivacaine are not used as a surface anesthetic.
- o Phase-II blockade is seen with Sch.
- * Maximum respiratory depression is seen with morphine, fentanyl (+++) & minimum with pentazocine.
- o Shortest acting non-depolarising muscle relaxant - Mivacurium
Shortest acting muscle relaxant : Sch.
- o **Mendelson syndrome** - Regurgitation of gastric contents causes aspiration pneumonitis
- o **Head tilt - chin lift maneuver:**
 - Used during assisted ventilation to secure airway.
 - C/ind in cervical spine injury
- Jaw thrust technique:** Can be used in cervical spine injury where head tilt should not be done.
- * **Sellick's manoeuvre:** To prevent regurgitation pressure is applied on cricoid cartilage which compresses oesophagus against vertebral column. This is done during rapid sequence intubation.
- o **TRUP manoeuvre:** Pressure over thyroid cartilage (by pressing it rt., post. & upward). Used to aid in intubation.
- o **Helmich's manovre:** Used for FB removal. Sudden pressure applied from back of the pt. by both hands below the costal cartilage.
- * **Breur Lockguard reflex:** Light anaesthesia & cervical dilatation (eg during anal stretching) can initiate parasympathetic overactivity causing laryngospasm, bronchospasm, bradycardia & even cardiac arrest.
- * Causes of sudden ↓ in end tidal volume in anaesthetised pt.
 - * Low CO, venous air embolism, circuit disconnection
 - * Pulmonary embolism
 - Venous air embolism
 - Circuit leak
 - Extubation
 - Cardiac arrest
- * Post-operative shivering is seen with:
Halothane (m/c), cyclopropane, thiopentone sodium, ether.
- o Drug used for treatment of post-operative shivering ---

pethidine - tramadol, clonidine, dexamethasone

* Indications for endotracheal intubation - maintenance of a patent airway, to provide IPPV, pulmonary toilet.

o **Induced hypotension**

- Drug - sodium nitroprusside NTG, Trimethopran, Arphonod

Spinal/epidural block

✓ β -blockers (Esmolol or propranolol)

✓ Inhalational agent - Isoflurane m/c, halothane, enflurane

✓ Positioning of patient ✓

* World anaesthesia day is on 16th october. On 16th oct 1846 ether was used first time.

o Smoking should ideally be stopped by 6-8 wks before surgery (Time required to increase ciliary motion). If smoking is stopped within 24 hr, decrease carboxy Hb can cause shift to right.

SOME IMP. NEGATIVE POINTS

- o NOT caused by atropine in pre-anesthetic medication --- Bronchoconstriction
- o NOT caused by Ipratropium bromide --- Bronchoconstriction
- o NOT a vasodilator LA --- Cocaine
- o NOT used in clearing airway --- Head lift
- o Bag and mask ventilation is NOT indicated in --- Diaphragmatic hernia, MAS.
- o Drug NOT useful for induction in infants --- Morphine
- o NOT true about pneumatic Anti-shock garments --- \uparrow CO
- o NOT used as surface anesthetic --- Procaine & Bupivacaine
- o NOT used as in Beir's block --- Bupivacaine
- o NOT used for controlled ventilation --- Mapelson A system or Magill circuit

* Flat capnogram is NOT seen in --- Bronchospasm

- o A pt with sickle cell trait is posted for surgery in left arm. NOT to do is --- IVRA (Intravenous regional anesthesia)
- o NOT true of xenon anaesthesia --- Slow induction and slow recovery.
- o NOT an adverse effect of neural opioid --- Itching, low BP, nausea, vomiting.
- o Factors that do not effect MAC are --- Sex-male or female
Thyroid disease.

CLINICAL VIGNETTES

* A 5 year old boy is suffering from Duchenne muscular dystrophy. He has to undergo tendon lengthening procedure. The most appropriate anaesthetic agents would be :

[AIPGMEE2003, DNB HRH Delhi' 08]

A. Induction with i.v. thiopentone and N_2O : and halothane for maintenance

B. Induction with i.v. suxamethonium and N_2O : and O_2 for maintenance

C. Induction with i.v. suxamethonium and N_2O : and halothane for maintenance

D. Induction with propofol and N_2O and O_2 for maintenance
(Ans.: D. Induction with propofol and N_2O and O_2 for maintenance)

DMD patients are susceptible for malignant hyperthermia so scoline and all volatile agents should be avoided, while N_2O and propofol are safe. Suxamethonium is ruled out.)

* A 5 year old is scheduled for strabismus (squint) correction. Induction of anaesthesia was uneventful. After conjunctival incision as the surgeon grasps the medial rectus, the anaesthetist looked at the cardiac monitor. Why did he do that? [AIIMS 2002]

A. He wanted to check the depth of anaesthesia

B. He wanted to be sure that the BP did not fall

C. He wanted to see if there was an oculocardiac reflex

D. He wanted to make sure there were no ventricular arrhythmias accompanying incision

(Ans.: C. He wanted to see if there was an oculocardiac reflex)

Oculocardiac reflex is a trigeminovagal reflex, afferents of which are carried out by trigeminal n. and efferents are mediated by vagus. It is seen during ocular surgery either d/to traction on eye m/s or d/to compression or stretching / pull on eye muscles. T/t includes stop stimulation, inj atropine, increase depth of anaesthesia, infiltration of LA in m/s, and retrobulbar block.

* A 6 year old child was posted for elective urological surgery under general anaesthesia. He refuses to allow the anaesthetist for an i.v. access. The best inhalational inducing agent in this child would be:

[AIIMS May 2004]

A. Sevoflurane

B. Methoxyflurane

C. Desflurane

D. Isoflurane

(Ans.: A. Sevoflurane)

- ❑ A 38 year old man is posted for extraction of last molar tooth under GA as a day care surgery. He wishes to resume his work after 6 hours. Which of the following induction agent is preferred-

[AIPGMEE2003, DNB HRH Delhi' 08]

- A. Thiopentone sodium B. Ketamine
C. Propofol D. Diazepam

(Ans. :C. Propofol)

Drugs preferred in day care surgery are : Propofol, desflurane, atracurium

- ❑ A 70 year old man is posted for a surgery which is likely to last 4-6 hours. The best inhalational agent of choice for maintenance of anaesthesia in such a case is:

[AIIMS May' 2004]

- A. Methoxyflurane B. Ether
C. Trilene D. Desflurane

(Ans. D: Desflurane)

Rapid onset and rapid offset of anaesthetic effect is seen with Desflurane

- ❑ A 30 year old female with coarctation of aorta is admitted to labour room for elective LSCS. Which of the following is anaesthetic technique of choice : [AIIMS Nov'2005]

- A. Spinal anaesthesia B. Epidural anaesthesia
C. General anaesthesia D. LA with nerve block

(Ans. C. General anaesthesia)

Some cardiac lesions, such as *aortic outflow obstruction*, *right to left shunts*, ↓ venous return, and ↓ systemic resistance are so grave that they make regional epidural and spinal anesthesia hazardous. GA has rapid induction, less hypotension, better airway and ventilation, better recovery. So GA is preferred in patient with CoA.

- ❑ A 20 year old female presented with early pregnancy for MTP in day care facility. Which of the following induction agent is preferred-

[AIIMS May' 2006, DNB HRH Delhi' 08]

- A. Thiopentone B. Ketamine
C. Propofol D. Dizepam

(Ans. :C. Propofol)

Propofol is preferred for day care surgery

Only agents which are rapidly eliminated are used for this purpose; e.g. propofol for induction of anaesthesia, alfentanil, renifentanil, N₂O, isoflurane, sevoflurane or desflurane.

- ❑ A severely ill patient was maintained on an infusional anaesthetic agent. On day 2 of admission he started deteriorating. The most probable culprits is/are

[PGI 1999, JIPMER 2004]

- A. Etomidate B. Opioid
C. Propofol D. Barbiturates

(Ans. :C. Propofol)

Propofol infusion syndrome: Seen after 48 hours of continuous infusion of propofol in ICU. Found in cases of cardiomyopathy, rhabdomyolysis, and bradycardia

- ❑ A 21 year old female with a history of hypersensitivity to neostigmine is posted for an elective LSCS under GA. Muscle relaxant of choice in this patient is-

[AIIMS May' 2004]

- A. Pancuronium B. Atracurium
C. Rocuronium D. Vecuronium

(Ans. B. Atracurium)

Atracurium is metabolized by Hoffman's elimination, so it does not require reversal of N-M blockade with neostigmine

- ❑ A patient was administered epidural anaesthesia with 15ml of 1.5% Lignocaine with adrenaline for hernia surgery. He developed hypotension and respiratory depression within 3 minutes after administration of block. The most common cause would be :

[AIIMS May'07]

- A. Allergy to drug administered.
B. Systemic toxicity to drug administered.
C. Patient got vasovagal shock.
D. Drug has entered the subarachnoid space.

(Ans. D. Drug has entered the subarachnoid space)

Epidural anesthesia/ peridural anesthesia.

During epidural anesthesia there occurs certain complications. One of which is total spinal. It occurs if by mistake, dura is punctured during injection and such large volume of drug is injected into subarachnoid space. Manifests by marked hypotension, bradycardia, apnea, dilated pupil and unconsciousness.

Also know

Other drug used for epidural block

- Lignocaine, bupivacaine
- Morphine, fentanyl, tramadol

Site of action of opioid after intrathecal and epidural administration

- Opioid after diffusion through meninges reaches the spinal cord where they bind opioid receptors present in *substantia gelatinosa of dorsal horn cells*.
- Site of action of LA is *anterior and posterior nerve roots*.

- A 6 month old child is suffering from patent ductus arteriosus (PDA) with congestive cardiac failure. Ligation of ductus arteriosus was decided for surgical management. The most appropriate inhalational anesthetic agent of choice with minimal hemodynamics alteration for induction of anesthesia is:

[AIIMS may'07]

- | | |
|----------------|---------------|
| A. Sevoflurane | B. Isoflurane |
| C. Enflurane | D. Halothane |
- (Ans.: A. Sevoflurane)

Induction agents in children and patient profile

Sevoflurane is inhalational agent of choice in children for induction. It is costly, so use is restricted. Cardiac output is minimally depressed.

Halothane also used for induction in children but it decreases cardiac output, causes bradycardia due to direct myocardial depressant effect. It is cheaper so used frequently for induction in children, but its effect on heart limits its use in patient with PDA.

Isoflurane is inhalational agent of choice for cardiac surgery but is irritant, so patient compliance is very poor. It is not used for induction of anaesthesia but for maintenance of anaesthesia.

- A 5 year old child is suffering from cyanotic heart disease. He is planned for corrective surgery. The induction agent of the choice would be:

- | | |
|----------------|---------------|
| A. Thiopentone | B. Ketamine |
| C. Halothane | D. Midazolam. |

(Ans: Ketamine)

TOF is cyanotic heart disease.

The goals of anaesthetic m/m in patients with TOF is to maintain intravascular volume and systemic vascular resistance (SVR)

"Ketamine is commonly used induction agent because it maintains or \uparrow SVR and therefore does not aggravate the right to left shunt".

- A 30 year old man who was recently started on haloperidol 30 mg/day developed hyperpyrexia, muscle rigidity, akinesia, mutism, sweating, tachycardia and increased blood pressure. The investigations showed increased WBC count, increased Creatinine Phosphokinase. There is no history of any other drug intake or any signs of infection. The most likely diagnosis is:

[AIIMS May'06]

- | |
|------------------------------------|
| A. Drug overdose |
| B. Neuroleptic Malignant Syndrome. |
| C. Drug induced Parkinsonism |
| D. Tardive Dyskinesia. |
- (Ans.: B. Neuroleptic Malignant Syndrome)

Neuroleptic Malignant Syndrome

- It occurs with high dose of potent antipsychotics. Symptoms develop within first 2 week of an antipsychotic drug t/t. NMS is a catatonia like state manifested by extrapyramidal signs. Blood pressure changes, altered consciousness, and hyperpyrexia
- It should be considered in d/d of malignant hyperthermia
- Patient develops marked rigidity, immobility, tremor, fever, semiconsciousness, Fluctuating BP and heart rate (Tachycardia and increased BP).
- Myoglobin may be presents in blood (Increased creatinine phosphokinase). Elevated creatine kinase and leukocytosis with a shift to left are present early in about half of cases.
- T/t
 - Stop antipsychotic & give i/v dantrolene
 - Bromocriptine (Anticholinergics do not help)

- A 16 yr male with exostrophy of bladder with chronic renal failure was admitted for bladder reconstruction. Anesthetic of choice would be.

[AIIMS Nov'09; AIPGMEE'10]

- | | |
|----------------|---------------|
| A. Pancuronium | B. Vecuronium |
| C. Rocuronium | D. Atracurium |
- (Ans. D. Atracurium)

Atracurium is safe in both liver and renal d/s patients as it is metabolized by Hoffman's degradation (non- enzymatic degradation).

- A female was posted to OT for laparotomy for surgery of ileal perforation for which rapid intubation was done. Immediately after intubation her EtCO_2 was raised and on auscultation breath sounds were ↓ on her left side. What is the most probable cause? [AIPGMEE'10]

A. Esophageal intubation
B. Bronchospasm
C. Endobronchial intubation on right side
D. ETT blocked

(Ans. C. Endobronchial intubation on right side)

EtCO_2 is a good indicator of ETT status.

- ETCO_2 becomes zero in --- esophageal intubation, pulmonary venous air embolism (sudden fall in EtCO_2).
- Flat capnogram is seen in --- Intraoperative displacement of ETT, disconnection of ETT, ventilation failure

- ETCO_2 becomes high in --- Exhausted soda lime or defective valves of closed circuit, malignant hyperthermia (upto 100 mmHg)

In bronchospasm and ETT blockade there is slow rise of EtCO_2 .

Accidental intubation on right side is common. ETT goes in right main bronchus and it will produce obstructive curve and rise of EtCO_2 .

- 42. A 65 yr old male known hypertensive, is scheduled for laparoscopic cholecystectomy under general anesthesia. Which of the following induction agent is contraindicated in this patient? [AIPGMEE'11]

A. Propofol
C. Etomidate

B. Ketamine
D. Midazolam

(Ans.: B. Ketamine)

Ketamine ↑ BP and HR

- An Anesthesia senior resident is performing epidural block. While injecting patient becomes aphonic and loses consciousness. The immediate diagnosis is:

[AIPGMEE'11]

A. Anaphylactic reaction
C. Vasovagal attack

B. Total spinal
D. Intravascular injection.

(Ans. B. Total spinal)

Total spinal is a rare complication manifested by profound hypotension, apnoea, unconsciousness and dilated pupils

- A 70 kg old athlete was posted for surgery. Patient was administered Succinylcholine d/to unavailability of vecuronium. It was administered in intermittent dosing. (total 640mg). During recovery patient was not able to respire spontaneously and move limbs. What is the reason:

A. Pseudocholinesterase deficiency increasing action of Sch block.
B. Phase 2 blockade produced by Sch
C. Undiagnosed muscular dystrophy and myopathy
D. Muscular weakness d/to fasciculations produced by succinylcholine.

(Ans. B. Phase 2 blockade produced by Sch)

In Sch, depolarising block can be changed to phase 2 block by administration of a dose 7-10mg/kg. Tetanic fade and train of four fade appears.

- Which of the following monitoring tool gives you the best recognition of intraoperative myocardial ischemia:

A. Electrocardiograph
B. Intra arterial pressure
C. CVP
D. Transesophageal echocardiography

(Ans. D. Transesophageal echocardiography)

- Inotrope of choice for intraoperative management of right heart failure due to pulmonary hypertension:

[AIPGMEE'11]

A. Dopamine
B. Isoprenaline
C. Milrinone
D. Halothane
(Ans.: C. Milrinone)

- NOT a definite airway : [AIPGMEE'11]

A. Orotracheal intubation
B. Nasotracheal intubation
C. Laryngeal mask airway
D. Cricothyroidectomy
(Ans.: C. Laryngeal mask airway)
LMA is supraglottic airway device.

NOTES

POST-OPERATIVE CARE OF PATIENTS

1. Patient Assessment

2. Vital Signs Monitoring

3. Pain Management

4. Fluid Management

5. Wound Care

6. Patient Education

7. Discharge Planning

8. Documentation

9. Communication

10. Patient Safety

11. Quality Improvement

12. Research

13. Ethics

14. Professionalism

15. Leadership

16. Teamwork

17. Patient-Centered Care

18. Evidence-Based Practice

19. Continuous Learning

20. Patient Satisfaction

21. Hospital Accreditation

22. Regulatory Compliance

23. Risk Management

24. Infection Control

25. Patient Safety Culture

26. Patient Safety Incident Investigation

27. Patient Safety Reporting

28. Patient Safety Training

29. Patient Safety Audit

30. Patient Safety Improvement

APPROACH TO A COMATOSE PATIENT

M/m Steps in Comatose Patients

First priority is ABC Airway, Breathing, Circulation

2010 guidelines recommend use of C-A-B sequence in field.

Airway & breathing

- Open airway by *triple manueuvre* **head tilt, chin lift** and **jaw thrust** (use only **jaw thrust** if cervical spine injury is suspected)
- Oral airway may be used only if atraumatic insertion is possible.
- Early intubation using rapid sequence (RSI) with full stomach precautions.

Indications for intubation in comatose patient include –

- Glasgow coma scale < 8.
- Inability to maintain airway patency/protection.
- Impaired oxygenation or ventilation.

Circulation

Assess circulatory status. If in shock, treat along standard guidelines with bolus of isotonic fluid and vasopressors as indicated.

Blind nasal intubation is indicated in

- TM joint ankylosis
- Trismus (tetanus, quinsy)
- Neck contracture

In case of Head injuries

Initial assessment must follow ATLS guidelines with an initial primary survey, alongwith resuscitation, followed by a secondary survey then definitive management. **Cervical spine must be immobilized** during the initial assessment or more simply : **airway** (first)→ **breathing** → **circulation** → **disability** and **exposure**. Rush to the emergency with OT set up.

Brain Death

Brain death is a state of cessation of cerebral function while somatic function is maintained by artificial means and the heart continues to pump. Prerequisite are

- Widespread cortical destruction (reflected by deep coma unresponsive to any stimulus)
- Global brainstem damage (Absent corneal reflex, Pupillary light reflex, oculovestibular reflexes)
- Complete apnea

Patient should not be hypothermic, hypoxemic, and hypotensive.

An **isoelectric EEG** may be used as a confirmatory test for total cerebral damage.

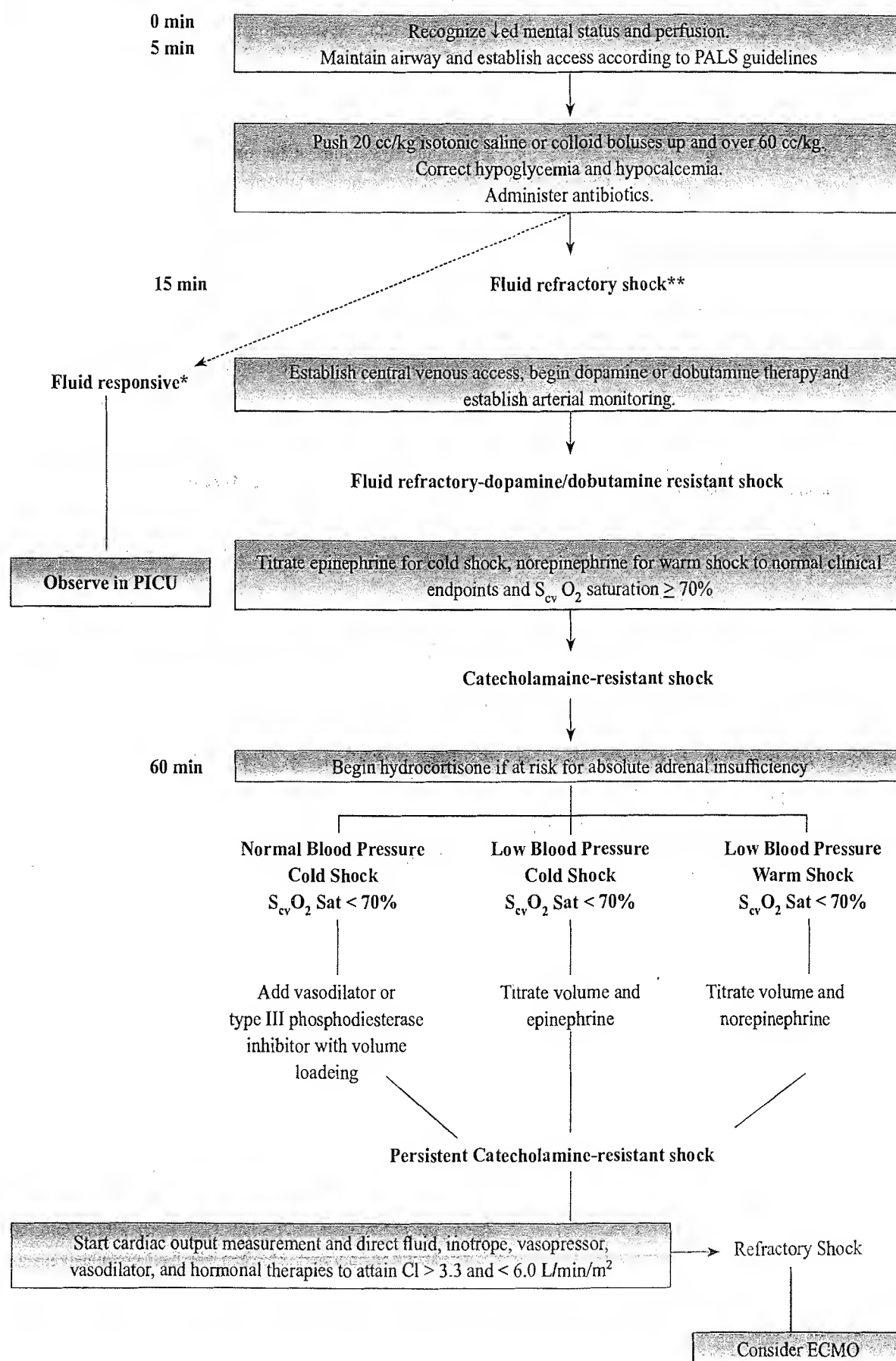
Hypoxic injury to brain

- Brain is extremely sensitive to hypoxia, and occlusion of its blood supply as short as 10 sec may produces unconsciousness .
- Vegetative structures are more resistant to hypoxia. Vegetative functions are relatively retained compared to intellectual functions
- Penumbra, is the area surrounding the most severe brain damage, or the area potentially salvagable if ischemia is reversed
- If circulation is restored within 3-5 min, full recovery may occur without sequelae
- Hippocampus (CA-1 neurons)** is most vulnerable to ischemic injury.
- Golden period to initiate thrombolytic therapy in thrombotic stroke is within first 2 hr after the onset of weakness/palsy.

Pupillary reaction based on the site of lesion

Site of lesion / cause	Pupil
Metabolic encephalopathies	Small reactive
Diencephalic	Small reactive
Midbrain	Mid position, fixed
Tectal	Large fixed, hippus
3rd nerve (uncal)	Dilated, fixed
Pons	Pinpoint

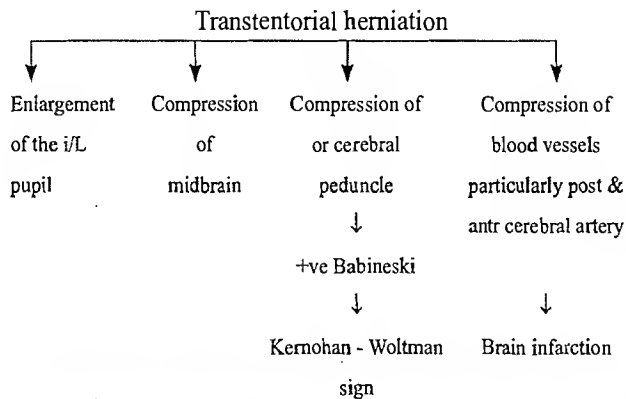
Management of Shock in children



Approach to pediatric shock. *Normalization of blood pressure and tissue perfusion;

**hypotension, abnormal capillary refill or extremity coolness. PALS, Pediatric Advanced Life Support; PICU, pediatric intensive care unit; CI, cardiac index; ECMO, extracorporeal membrane oxygenation.

→ Triad in pontine hemorrhage -- pin point pupils + loss of consciousness + hyperpyrexia



HEAD INJURY AND TYPE OF HEMATOMA

	Epidural	Subdural	SAH
1. Cause	Middle meningeal artery injury	Injury to cortical bridging veins	Berry aneurysm rupture, trauma
2. Crosses	Across dural attachment sutures	Do n't cross sutures	
3. CT Scan	Biconvex, Dense area	Crescent (Cocavo-convex) inner border concave	NCCT (Non contrast CT) is investigation of choice
4. Other	$\frac{2}{3}$ hyperdense, $\frac{1}{3}$ mixed appearance	1. Hyperdense (<2 wk) 2. Isodense (2-4wk) 3. Hypodense (>4 wk)	Four vessels (Both carotid & both vertebrals) DSA is investigation of choice for determining etiology Hallmark of SAH is blood in CSF detected by LP (Bloody tap in CSF).

Induced eye movements

Oculocephalic/Dolls eye response

- Should only be tested in unconscious patient
- Normal or positive response is conjugate deviation of eyes in opposite direction to which the head is turned.
- Negative response indicates brainstem lesion.

Oculovestibular response or caloric test

EAC is irrigated with cold water to induce convection currents in labyrinths. Nystagmus is fast component

There may be 3 type of response

1. Normal awake patient with intact brainstem - tonic deviation of both eyes to the side of cold water irrigation and nystagmus in the opposite direction. Side with the slow component towards irrigated ear and fast component towards midline.(acronym COWS)
2. Unconscious pt. with intact brainstem
Fast component abolished, eye move towards stimulus and remain toxically deviated for > 1 min.
3. Unconscious pt with brainstem dysfunction/brain dead pt.
There is no response to stimuli i.e. eyes remain in midline.

SHOCK

Hypovolemic shock : Classification

	Class 1	Class 2	Class 3	Class 4
Blood loss	<15% (750 ml)	15-30% (.8-1 litre)	30- 40% (1.5-2 litre)	> 40% (>2 litr.)
SBP	No change	No change	↓	↓↓
Pulse rate	Slight ↑	100-120	> 120, weak	> 120, thready
RR	N	↑	> 20	20-30
Capillary refill	Normal, 2 sec	> 2 sec.	> 2 sec.	Very delayed
Mental status	Alert	Anxious	Anxious + aggressive	Drowsy, confused unconscious

- Resuscitation of the trauma patient (pediatric /adult) begins with isotonic crystalloid, in a child 20ml/kg
- Urine output is the most important parameter of adequate tissue perfusion in a patient with shock
- PCWP or CVP is used to assess volume replacement in hypovolemic shock
- In children, **hydrocortisone** is indicated in septic shock in children with catecholamine resistance and suspected or proven adrenal insufficiency (children with severe septic shock and purpura , children who have previously received steroid therapies for chronic illness, and children with pituitary or adrenal abnormalities).

TRIAGE COLOUR CODING SYSTEM

- French word meaning to "sort" by priority or life-threatening nature of injury. Prioritize the patient for t/t and transport purpose.
- Retriage occurs when the status of a patient changes either to a worse condition or if they improve to a less life-threatening level.

Color Code	Nature of injury	Priority	Attention/Action
Red	Serious but salvageable life threatening injury/illness	1st	Immediate
Yellow	Moderate to serious injury/illness (but not immediately life-threatening) e.g. fractures	2nd	
Green	Walking -wounded	3rd	
Blue	Potentially fatal injuries, unsalvageable, some vital signs	4th	
Black	Clearly deceased, no vital signs	5th	

TRAUMA

Trauma : Basic POINTS

- Following trauma level of stress hormone is ↑ed i.e. Glucocorticoids, Glucagon, ADH, GH etc.
- M/c abdominal organ injured in blunt trauma abdomen is spleen and in penetrating trauma-- small intestines
- Seat belt causes injury to duodenum
- Prox. Jejunum and ileocecal junction are commonly injured among intestine in blunt abd. Injuries.
- Marshall's triad in blast injury:
Small contusion + Punctate abrasion + Puncture laceration.
- CECT is best for blunt trauma abdomen.
- CVP monitoring is ideal to determine fluid administration. Not in case of abdominal trauma as raised intraabdominal pressure contributes to CVP.
- TRISS determines the probability of survival (Ps) of a patient from ISS and RTS using the formula $Ps = 1/(1+e^{-b})$
- Score for assessing outcome of SAH (subarachnoid hemorrhage) --- HESS and Hunt score

FLAIL CHEST

- Results from # of at least 2 sites of 3 adjacent ribs.
- Often accompanied by physiological dearrangements.

- D/g: by inspection asymmetrical chest wall movement and paradoxical movements are seen in spontaneously breathing patient.
- T/t: Mainly ventilatory support. Mechanical ventilation should be started if PaO₂ is <70 mmHg.
- Surgical stabilization (preferably internal) is advocated now a days.

Scoring Systems for Critical Patients

Glasgow coma scale (GCS)

- Most widely used
- Originally used to predict the outcome after head injury in adults.
- Normal score is 15
- Based on Eye opening, verbal response and motor response (E4V5M6)

Revised trauma score -

Includes GCS + RR + SBP

Other scoring systems

- APACHE (Acute Physiology And Chronic Health Evaluation)
- MPM (Mortality Probability Model)
- SAPS (Simplified Acute Physiology Score)
- PRISM III (Pediatric), PIM 2 score

- APACHE II scoring system is the sum of acute physiology scores (vital signs, oxygenation, lab values), GCS, age and chronic health points. Worst values during the first 24 hours in the ICU should be used.
- TRISS score (Trauma and injury severity score) includes --- ISS + RTS + Age.
- Modified Child- Pugh score is used for cirrhosis of liver in adults.
- CATS is a Canadian system

HEAD INJURY

- Severe head injury is a/w a stress response c/by hyperglycemia, which worsens the outcome.
- Prognosis in head injury patient is best given by GCS (Glasgow coma score).
- Hypothermia is cerebroprotective.
- IPPV to produce moderately low normal arterial CO₂ (PaCO₂ 35 mmHg) is a/w ↓ Cerebral swelling and ↓ ICP.

• *Factors adversely affecting the prognosis in head injury patient*

1. Factors which ↓ CBF --- Cerebral ischemia
2. Hyperglycemia has always a bad prognosis in patients of head injury
3. Factors which ↑ ICP --- Cerebral vasodilatation by hypercapnia

• *Factors a/w good prognosis in head injury patient*

1. Factors which ↑ CBF --- Hemodilution, ↑ MAP and ↑ CPP
2. Factors which ↓ ICP (intra cranial pressure) --- Hyperventilation.
3. Hypothermia

• In a patient of head trauma with unexplained hypotension evaluation of upper cervical spine is must.

INTRA CRANIAL PRESSURE (ICP)

- Normal ICP is 2-12 mmHg
- Early signs of ↑ ICP include ---- drowsiness and ↓ level of consciousness.
Change in level of consciousness is the earliest and m/c manifestation of raised ICT in a patient of head injury.
- Gold standard method for monitoring ICP ---- Intraventricular catheter
- T/t
 - All potentially exacerbating factors must be eliminated (i.e. hyperthermia, hypercarbia, high mean airway pressure in ventilators, hypoxia)
 - Emergent T/t of raised ICP is most quickly achieved by **temporary hyperventilation**, which causes vasoconstriction and reduces cerebral blood volume.
 - Mannitol, 3% saline,
 - Drainage of CSF. Head up or reverse Trendelenberg's position.
 - High dose barbiturates and hypothermia for refractory cases.

→ *Segment of spine which must be evaluated in case of unexplained hypotension in a head injury patient --- upper cervical*

→ *In head trauma and stroke cytotoxic edema is seen.*

→ *Steroids have been shown to be highly effective in reducing vasogenic edema (around brain tumors/other CNS lesions). In traumatic brain injury steroids have not been effective in reducing ICP/ improving neurologic outcome rather adds damage by causing hyperglycemia.*

RESPIRATORY FAILURE

Type of respiratory failure	Subtype	ABG	Example
TYPE I ($\text{PaO}_2 < 60$; $\text{PaCO}_2 < 50$ mm Hg)	Acute	$\text{PaO}_2 \downarrow \downarrow$ $\text{PaCO}_2 \leftrightarrow$ $\text{pH} \leftrightarrow \text{or} \uparrow$ $\text{HCO}_3 \leftrightarrow$	Asthma, Pulmonary embolus, Pulmonary edema, ARDS, Pneumothorax, Pneumonia
	Chronic	$\text{PaO}_2 \downarrow$ $\text{PaCO}_2 \leftrightarrow$ $\text{pH} \leftrightarrow$ $\text{HCO}_3 \leftrightarrow$	Emphysema Lung fibrosis Lymphangitis carcinomatosa R - L shunts Anemia
Type II ($\text{PaO}_2 < 60$; $\text{PaCO}_2 > 50$ mm Hg)	Acute	$\text{PaO}_2 \downarrow$ $\text{PaCO}_2 \uparrow$ $\text{pH} \leftrightarrow$ $\text{HCO}_3 \uparrow$	Severe acute asthma Acute epiglottitis FB inhalation, Respiratory ms paralysis, Flail chest injury Sleep apnea Brain stem lesion Narcotic drugs
	Chronic	$\text{PaO}_2 \downarrow$ $\text{PaCO}_2 \uparrow$ $\text{pH} \text{ or } \leftrightarrow$ $\text{HCO}_3 \uparrow$	Chronic bronchitis, Primary alveolar HTN, Kyphoscoliosis, Ankylosing spondylitis

Type III respiratory failure

- Is the result of lung atelectasis. Also called **perioperative** respiratory failure.
- Seen after G.A., ↓ in FRC leads to collapse of dependent lung units.

Type IV respiratory failure

- Occurs bec/of hypoperfusion of respiratory muscles in patients of **shock**.
- Patient of shock often suffer resp. distress d/to pulmonary edema, lactic acidosis & anemia.

ARDS (Adult Respiratory Distress Syndrome or " Shock lungs ")

- Predisposing factors are – Septicemia, fat embolism, multiple transfusions.

- **Causes are** – Trauma, acute pancreatitis, severe falciparum malaria, amniotic fluid aspiration, Gram negative sepsis, smoke inhalation/ Cl_2 gas
 - **Patho** – pulmonary edema, stiff lungs ('baby lung'), fibrosis, alveolar damage.
 - **Diagnostic criteria of ARDS are ---**
 1. $\text{PaO}_2/\text{FiO}_2$ ratio <200 mmHg,
 2. Onset acute, presence of predisposing factor,
 3. B/l interstitial infiltrate,
 4. Absence of left atrial hypertension.
 - **Lab/f**
 - Hypoxemia, hypercapnia, pulmonary HTN, PAWP normal
 - Normal PCWP in ARDS distinguishes it from cardiogenic pulmonary edema
 - Uremic lungs are char/by diffuse alveolar injury & pulmonary edema
 - **T/t**
 - Lung protective ventilation (low tidal volume and high PEEP)
 - Oxygen, treat the cause
 - Use of newer modes of ventilation like partial liquid ventilation, inverse I: E ratio, prone position ventilation, APRV, ECMO
- "Wet lung" term is used for lungs in CHF
- Acute life threatening pulmonary edema is treated by --- Morphine, frusemide, CPAP, oxygen, Glycerol trinitrate etc.

VENTILATORS

Change in settings for Correction of ABG

When PaO_2 falls Interventions are ---	When PaCO_2 is high Interventions are ---	When PaCO_2 is low the interventions are ---
$\uparrow \text{FiO}_2$ $\uparrow \text{PIP}$ \uparrow Inspiratory time $\uparrow \text{PEEP}$	$\uparrow \text{RR}$, $\uparrow \text{TV}$ $\uparrow \text{MV}$	$\downarrow \text{RR}$, $\downarrow \text{TV}$

→ When PaO_2 is high desired ventilator settings to lower PaO_2 are --- $\downarrow \text{PEEP}$, $\downarrow \text{PIP}$, $\downarrow \text{FiO}_2$

- Negative pressure ventilation is currently not in use.
- Combination of mandatory and spontaneous breath is intermittent mandatory ventilation (IMV) or SIMV
- Most popular mode of ventilation is IPPV & CPAP in

neonates.

- **Indications of CPAP are -**
 - Inability to maintain $\text{PaO}_2 > 50$ mm Hg in spite of FiO_2 60%.
 - $\text{PH} < 7.2$
 - $\text{PaCO}_2 > 50$ mm Hg
 - Prolonged apnea of prematurity
 - Severe tachypnea and exhaustion.
- **Modes allowing for spontaneous ventilation**
 - IMV
 - SIMV
 - PSV/CPAV
 - HFV (High frequency ventilation)
 - APRV (airway pressure release ventilation).
- IPPV is also k/as controlled mechanical ventilation
- HFV and APRV are used in ARDS patients.
- CPAP is M/c used form of mechanical ventilation in children.

Weaning from ventilators

- Modes used for weaning from ventilators are SIMV, IMV, CPAP, PSV, SBT, T piece
- **Criteria to met before initiating weaning in children**
 - Alert mental status
 - Good cough and gag reflexes
 - Core temperature $<38.5^\circ\text{C}$
 - pH 7.43 - 7.47
 - $\text{PaO}_2 > 60$ mmHg
 - FiO_2 0.5 or less
 - $\text{PEEP} \leq 7$
 - No clinical need to \uparrow support in last 24 hours
 - No planned operative procedures requiring heavy sedation in next 12 hours.
- **I : E ratio**
 - Normal I:E ratio is 1:2
 - During artificial ventilation, it should be set at 1 : 2 to ensure complete expiration.
 - In HMD & ARDS, the time constant is \downarrow ed and the desired I : E ratio is set at 1.5 : 1 or upto 2 : 1 (K/as Inverse IE ratio)
 - In MAS/obstructive airway d/s/ asthma expiration is prolonged, time constant is \uparrow ed and the desired I : E ratio is 1 : 2.7 or up to 1 : 4
- **PEEP**
 - Is generally kept between 4-6 cm of water it should be kept on the lower side in \uparrow ICT, pneumothorax, hypovolemia, pericardial tamponade.
 - Is used to overcome physiological resistance of circuit,

& in case of pulmonary edema.

- **PIP**
 - Should be kept below 30 cm of water
- **HFV**
 1. High frequency PPV, HFoscillations and HF jet ventilation modes are available .
 2. Indications are : Bronchoscopy, bronchopleural fistula, and cricothyroid membrane puncture, for which jet HFV is used in emergency.

PULSE OXIMETRY

- Is a simple and non-invasive method of monitoring the % of Hb which is saturated with oxygen (measures oxygen saturation not O₂ content)
- Based on the principle of **Beer-Lambert law**, which states that the concentration of an unknown solute in a solvent can be determined by light absorption.

$$L(\text{out}) = L(\text{in}) - DCA$$
- Wave length of 660 nm (red) and 940 nm (infrared) are used by photodetector for absorption characteristics of two Hb, reduced Hb and oxy Hb respectively.

- Pulse oximeter falsely detects O₂ saturation of 85% in methemoglobinemia.
- Carboxy hemoglobin will be interpreted as oxy-Hb by the photodetector of pulse oximeter (because carboxy Hb and oxy Hb have very similar absorbancies at 660 nm) thus ordinary pulse oximeter will over estimate the saturation in presence of carboxy-Hb.
- Arterial O₂ should be maintained b/n 92-96 % for acute condition & 88-92% for chronic conditions to prevent ROP

Potential inaccuracy of pulse oxymetry may be d/to :-

- Dyshemoglobinemia (Carboxy-Hb, met-Hb)
- Dyes and pigments (methylene blue), nail polish, bilirubin
- Low perfusion
- Interference from external light sources and optic shunt
- Movement interference
- In Methemoglobinemia O₂ saturation is falsely seen around 85% in pulse oximeter
- **Central cyanosis** is seen when level of
 Reduced Hb > 5gm% or
 Methemoglobin > 1.5 gm% or
 Sulf-hemoglobin > .5 gm% or
 O₂ saturation < 85%

CARDIAC ARREST AND CPR

- **M/c type of ECG rhythm at the time of cardiac arrest**
 - in children --- Pulseless electrical activity
 - and in adults ---VT without pulse
- **M/c cause of cardiac arrest in children is --- hypoxia** (rescue breaths are more effective)
- **M/c cause of cardiac arrest in adult is --- cardiac causes** (chest compression are more effective)
- In hospital setting, tracheal intubation is the preferred method of maintaining a patent airway in an unconscious patients with cardiac arrest. Prior to intubation an oropharyngeal airway can be used to prevent fall of tongue. Outside hospital settings BMV is still preferred.
- The standard ventilation bags used during CPR have a volume of 1600 mL
- To minimize the circulatory adverse effects of hyperventilation, avoid lung ventilation > 10 breaths/min.
- Any dextrose containing fluid should be avoided.
- In CPR
 DOC for asystole in CPR : Adrenaline
 DOC for bradycardia in CPR : Atropine
- The first step in CPR is circulation now a days (C→A→B Circulation→airway→breathing sequence)
 1. A clear airway is obtained by supine positioning and opening the airway by head tilt, chin lift, or jaw thrust maneuver.
 However, in case of trauma (or head injury) only jaw thrust is used to open the airway, Head tilt and chin lift should not be used.
- **AHA guidelines for CPR**

	Neonates & < 2 months	Infants/ children	Infant/ children	Adult
Compression	90/min	~ 100/min	~100/min	≥100/min
Compression to ventilation ratio	3:1 (2 rescuer)	30:2 (single rescuer)	15:2 (if two rescuer present)	30:2 (or 15:1)

Newer recommendations in CPR

- Chest compression to ventilation ratio is 30:2
- 1-shock strategy instead of 3- shock strategy.
- Sequence is now CAB Compression → airway→breathing.
- Look,listen,and feel has been removed.
- Glucose and calcium containing solutions are to be avoided

during CPR as hyperglycemia and hypercalcemia may cause neuronal damage.

Advanced Life Support (ALS or ACLS)

Defibrillation :

- DC cardioversion is TOC for pulseless V- tach and V-fib
- Recommended energy level for the first shock is 200 joules for biphasic shocks & 360 joules for monophasic shocks. In children it is 2J/kg

Drugs administered during CPR

- Avoid ET route, as dose of ET drugs are still not confirmed.
- *Drugs which can be given via endotracheal routes are --- atropine, epinephrine, vasopressin, lidocaine*
- **Epinephrine** is recommended for most cases of pulseless cardiac arrest including those d/to asystole, pulseless ECG. Atropine is adjunct
- IV Amiodarone is now recommended for cases of V-fib and pulseless V-tach that are refractory to defibrillation and vasopressor drugs.
- IV calcium gluconate is indicated if --- there is hypocalcemia, CCB toxicity, and electromechanical dissociation
- An increase in end tidal CO_2 ($\uparrow \text{EtCO}_2$) is the predictor of successful outcome
- Peripheral veins are preferred to central vein as it do not require interruption of CPR. Vascular/ Intraosseous route is preferred over tracheal route for drug administration.

Acute Coronary Syndrome (ACS)

- Oral / i.v. nitroglycerine is indicated to relieve chest pain d/to unstable angina or ACS a/w HTN. Morphine is the DOC for chest pain that is refractory to nitroglycerine

Acute Pulmonary Edema

- Nitroglycerine (sub-lingual) is most effective in reducing preload.
- Loop diuretics esp furosemide is being used for years. It acts by diuresis + venodilatation.
- Morphine can help in \downarrow ing COP.
- NPSV (Non-invasive pressure support ventilation) should be considered early. It \downarrow es preload & afterload and \uparrow es intrathoracic pressure.

Acute aortic dissection

- Clinical presentation can be mistaken as an ACS
- Pain is sharp and tearing/ ripping
- MRI is the diagnostic modality of choice
- HTN is treated by esmolol + nitroprusside. Labetolol is alternative for monotherapy
- **Fenoldopam** is a recent drug useful in aortic dissection
 - *Positive inotropic agents have no role in diastolic heart failure. Diuretic therapy can be counterproductive and may further impair ventricular filling and CO*
 - *Intra-aortic balloon counterpulsation pump (IABP) is used in selected cases of MI with cardiogenic shock that is refractory to hemodynamic drug support*

Central Venous Catheter

- M/c route of central venous catheterization is femoral vein.
- Catheter related sepsis is the m/c complication.

INTUBATION

Intubation is difficult in (Conditions a/w intubation failure are)--

1. Laryngeal edema
2. LTB
3. Epiglottitis

Orotracheal (endotracheal) intubation

- *Common method of endotracheal intubation is oro-tracheal approach.*
- *Rough guide to Tube size is*
 - 2.5 --- Preterm
 - 3.5 --- Full term healthy infant
 - 4 + Age in years /4) --- For children
 - 7.5 to 9 --- in adults

→ *Armoured ET tubes are cuffed tubes used in neurosurgery.*

Contraindications to Nasal Intubation

- Severe nasal/midface trauma
- Basilar skull #
- Patient taking anticoagulants or having h/o coagulopathy

Rapid sequence intubation (RSI)

- Done in full stomach patients.
- Indications are:
 1. Trauma patient with GCS of ≤ 8
 2. Significant facial trauma with poor airway control
 3. Burn patient with airway involvement and inevitable airway loss
 4. Respiratory exhaustion e.g. respiratory failure, near drowning, COPD with hypoxia, CHF.
 5. Non-fasting state (full stomach) in a patient requiring intubation.
 6. Prolonged seizures
 7. Drug overdose with altered mental status.
- *Sequence for normal anaesthesia :*
3-4 min pre -oxygenate \rightarrow I/v induction \rightarrow MR \rightarrow BMV \rightarrow Intubate
- *Sequence in full stomach patients:*
Preoxygenate \rightarrow I/v induction + Sedation \rightarrow Fast acting muscle relaxation (Sch or vecu /rocuronium) \rightarrow Apply cricoid pressure (Selik's maneuver) \rightarrow Intubate
Bag and mask ventilation (BMV) is contra- indicated
- Cuffed ET- tube should be used
- C/ind : significant facial edema, distorted laryngeal anatomy (post cancer pt), airway anomaly
- Drugs used for m/s relaxation --- Rocuronium > Vecuronium, Sch (scoline).
- *Emergency intubation is required in :*
High spinal injury

Practical Points

- The basilic vein is preferred to cephalic vein for PICC (peripherally inserted central catheters) because it is slightly larger than the cephalic vein
- Presence of a coagulation disorder is **not** a contraindication to placement of central venous catheter.
- Femoral vein is **not** recommended as a primary site for placement of central venous cannulation d/to risk of venous thrombosis.
- Peripheral venous catheter should be replaced every 3-4 days

PALS GUIDELINES

Pediatric advanced life support (PALS) guidelines are important in m/m of critical children

Important formulae in PALS to select

1. ET Suction catheter (Suction of ETT)
= Internal diameter (size) of ETT X 2 FG
2. Lip to carina length of ETT (Length of ETT)
= Internal diameter (size) of ETT X 3 cm
3. Size of ETT in children (Internal diameter)
= (Age in years/4) + 4 mm

Hypotension (low BP) is said if

- Systolic BP is <60 --- in newborn
- Systolic BP is < 70 + age \times 2 --- in 1-10 years children
- Systolic BP is < 90 --- in >10 years children, adults

In Pediatric assesment

- AVPU assessment include -- Alertness, Verbal response, response to pain, Unconsciousness
- SAMPLE assessment include -- Signs/symptoms, allergies, medications, past history, last meal, exposure to any toxins

ABCD of CPR in adults/ children are

- Airway
- Breathing
- Circulation
- Defibrillation

ABCDE of primary assessment of a pediatric patient

- Airway
- Breathing
- Circulation
- Disability
- Exposure

M/m and Action steps in an unresponsive/ critical child

- Sequence is : Asses \rightarrow Categorize \rightarrow Decide \rightarrow Act
- General assesment : PAT triangle
 - Appearance
 - Breathing
 - Circulation

Is there any action required (O_2 inhalation, CPR, BMV etc.) on the basis of general assessment ---Act

- Do primary assessment ABCDE (C-A-B now a days)
 1. Airway --- Is airway maintainable or not \rightarrow If not maintainable do head tilt chin lift maneuver (use only

jaw thrust if cervical spine injury is suspected), suction etc.

2. **Breathing** --- Check 5 things RR, chest movements, work of breathing, air entry, any added sounds
3. **Circulation** --- Check HR, pulses (both central and peripheral), temperature, sPO₂, CFT, BP.
Supportive evidence of circulatory status are --- skin, kidney and brain perfusion (look for mottling / colour of skin, urine output, mental status)
4. **Disability** --- Neurological status by ---
 1. AVPU assessment (alertness, verbal response, pain response, unconsciousness) for cortical function
 2. Pupillary response for cerebellar function
5. **Exposure** --- Includes complete head to toe examination

Categorize, decide and act on the basis of primary assessment

- Secondary assessment includes --- SAMPLE (Sign/symptoms, allergy, medication history, past history, last meal, exposure to any toxin etc.)

Decide and act on the basis of secondary assessment

IMPORTANT NEGATIVE POINTS

- Transtentorial herniation does NOT usually results in --- Ipsilateral hemiparesis
- NOT useful in management of acute pulmonary edema --- Digoxin
- NOT true of flail chest --- Paradoxical movements may not be seen in conscious patient.
- NOT included in APACHE score --- S. Calcium level
- Administration of glucose solution is not prescribed in --- Hx of unconsciousness.

CLINICAL VIGNETTES

- A 40 year old patient, who underwent bypass surgery for triple vessel disease 6 hours back, presents with signs of decompensated heart failure. O/E his PCWP is 18 mm Hg, cardiac output is 3L/min, and BP is 170/100 mmHg. Best initial t/t for this patient would be--
 - A. Diuretics
 - B. Vasodilators
 - C. Dobutamine

D. Dopamine

(Ans. Vasodilator therapy)

- A 40 year old patient presents with signs of decompensated heart failure. He has a recent H/O myocarditis. O/E his PCWP is 18 mm Hg, cardiac output is 3L/min, and BP is 120/82 mmHg. Best initial t/t for this patient would be--
 - A. Diuretics
 - B. Nitroprusside
 - C. Dobutamine
 - D. Dopamine
 (Ans. Dobutamine)

- A 40 year old patient after an episode of acute MI presents with signs of decompensated heart failure. O/E his PCWP is 18 mm Hg, cardiac output is 3L/min, and BP is 100/54 mmHg. Best initial t/t for this patient would be--
 - A. Diuretics
 - B. Nitroprusside
 - C. Dopamine in a dose 5 µg/kg/min
 - D. Dopamine in a dose > 10 µg/kg/min
 (Ans. Dopamine in a dose > 10 µg/kg/min)

Clue to the d/g or t/t are

M/m strategies for decompensated left sided heart failure are based on the BP of patient

Patient profile	Prior event	T/t
High PCWP, low CO, High BP	Bypass	Vasodilator t/t with nitroprusside/ nitroglycerine (↑CO by decreasing afterload)
High PCWP, low CO, normal BP	IHD, myocarditis, chr cardiomyopathy	Inodilators t/t with dobutamine/ milrinone (If PCWP does not improves, add furosemide)
High PCWP, low CO, Low BP (Cardiogenic shock)	Acute MI, pulmonary embolism, bypass, viral myocarditis	Dopamine in vasoconstrictor dose (> 10 µg/kg/min)

- Diuretics are useful in chronic heart failure
- Nisiritide is a recombinant human B-type natriuretic peptide which is a systemic vasodilator
- A 40 year old patient presents with signs of right heart failure following an episode of acute MI.

O/E his PCWP is 13 mm Hg, and BP is 86/46 mmHg. Best initial t/t for this patient would be--

- A. Infusion of IV fluids B. Nitroprusside
C. Dobutamine D. Dopamine

(Ans. Infusion of IV fluids)

T/t of diastolic/ right sided heart failure following an episode of MI (usually inferior wall MI) is guided by PCWP and RVEDV

- If PCWP is < 15 or the RVEDV is below 140mL/ m²
--- Infuse volume until PCWP or CVP increases by 5 mm Hg (reaches 20 mmHg)
- If PCWP is > 15 or the RVEDV is 140mL/ m² or higher--- start dobutamine @ 5 µg/ kg/ min

- A head injured patient, who opens eyes to painful stimulus, is confused and localizes to pain. What is his Glasgow coma Score? [AIIMS Nov'05]

- A. 7 B. 9 C. 11 D. 13

(Ans: C. 11)

Glasgow coma scale — includes EVM assesment

Eye opening :

- Spontaneous 4
- To speech 3
- To pain 2
- None 1

Best Verbal response :

- Oriented 5
- Confused 4
- Inappropriate words 3
- Incomprehensible sounds 2
- None 1

Best Motor response :

- Obeys 6
- Localizes 5
- Withdrawal 4
- Abnormal flexion 3
- Extensor response 2
- None 1

- A patient who sustained blunt trauma abdomen with Glasgow coma score 15, pulse rate 120/ mt, BP of 100/80 mmHg, management priority after ensuring breathing and ventilation include one of the following

- A. Establishment a good airway
B. Immediate blood transfusion

- C. IV fluids and a sample of blood for cross matching
D. Rush to operation theatre

[All India '09]

(Ans.C. IV fluids and a sample of blood for cross matching)

T/t protocol in blunt abdominal trauma

1. Primary survey --- CABDE

C = Circulation (establish i.v. line, check pulses, CFT, BP, Correct hypovolemia by crystalloids)

A = Airway maintenance (with cervical immobilization)

B = Assess breathing (ensure adequate ventilation, give oxygen, look for b/L air entry).

D = Disability (determine neurological status, AVPU assesment for cortical function, pupillary response for cerebellar lesion)

E = Exposure (Completely expose the patient and examine)

- In a patient of head trauma with unexplained hypotension one should look for evaluation of

- A. Upper cervical spine
B. Lower cervical spine
C. Thoracic spine
D. Lumbar spine

(Ans.A. Upper cervical spine)

[All India '09,AIIMS May'08, 09]

- A head injury patient is admitted. On examination he opens eyes on giving painful stimuli, there is inappropriate verbal response and he is able to localise pain. The Glasgow coma score for this patients is: [AIIMS Nov'09]

- A. 8 B. 10
C. 12 D. 14

(Ans. 10)

- A patient after THR post op day 2 develops chest pain, hypotension and respiratory distress. ECHO shows right ventricular motion abnormalities with TR. Most likely diagnosis is : [AIPGMEE'10]

- A. Pulmonary embolism B. Myocarditis
C. Acute MI D. Constrictive pericarditis.

(Ans. A. Pulmonary embolism)

Right ventricular motion abnormalities with TR on ECHO are suggestive of right ventricular dysfunction most likely secondary to pulmonary embolism. Pulmonary embolism is a known complication after THR.

Ejection fraction is affected and cardiac involvement is global in myocarditis and pericarditis.

- Q A 24 yr old male presents in the casualty with hollow viscous perforation peritonitis of 24 hrs duration and shock. After securing airway and breathing and starting IV fluid resuscitation, the next most appropriate management strategy would be----

[AIPGMEE'11]

- A. Shift the patient in OT and perform exploratory laparotomy under GA
- B. Immediately insert abdominal drain under LA and shift the patient in OT for exploratory laparotomy
- C. Immediately shift in OT for diagnostic laparoscopy and proceed under GA
- D. Stabilize the patient in casualty and correct electrolytes followed by exploratory laparotomy in OT under GA

(Ans. : A. Shift the patient in OT and perform exploratory laparotomy under GA)

- Q In an ICU patient, Right subclavian vein cannulation for CV line was done. Few hours later, he suddenly developed dyspnea, tachycardia, and hypotension. Chest examination revealed hyper-resonance on percussion, and decreased breath sounds on auscultation. Left sided breath sounds were minimally reduced Which of the following is likely diagnosis?

[AIPGMEE'12]

- A. Tension pneumothorax
- B. Traumatic hemothorax
- C. Catheter fracture
- D. Air embolism

[Ans. A. Tension pneumothorax]

Puncture of pleura → Tension pneumothorax is a common complication of subclavian line placement. Clinical signs are very much suggestive of pneumothorax.

NOTES

SLEEP & RELATED DISORDERS

REM & NREM Sleep

	REM Sleep	NREM Sleep
1. Also k/as	Paradoxical sleep or active/ deep sleep	Slow wave sleep, orthodox /quiet sleep
2. EEG	Delta wave in EEG	Theta wave
2. Autonomic hyperactivity	++ ↓ HR ↑ RR ↑ BP	↓ HR & ↓ RR, ↓ BMR
3. Brain O ₂ consumption	↑	Normal
4. GH secretion	↑	
5. Tone	↓ (esp in head / neck)	Normal
6. ↑ activity in	Pontine, amygdala, and anterior cingulate gyrus	Thalamo-cortical loop
7. Parasomnias	Narcolepsy, cataplexy, Nightmares (dream anxiety), Active dreaming, Penile erection (tumescence)	Most parasomnias are seen in stage IV (δ-sleep) e.g. Sleep/ night terrors (Pavor nocturnus), Sleep walking (Somnambulism), Sleep talking (Somniloqui), Bruxism (teeth grinding) in stage II, Enuresis (bed wetting), Head tossing (jactatio capitis) in stage 0, I

→ Barbiturates & MAO inhibitor reduce REM sleep while BZD's suppress stage 4 NREM. A single dose of BZD at bedtime is effective against stage 4 parasomnias.

→ REM sleep is c/by PGO spikes.

* NREM stage 2 is c/by sleep spindles and k-complexes

→ Muscle hypotonia is most characteristic of REM sleep which differentiates it from wakefulness.

* "Epworth sleepiness scale" is used to measure excess day time sleepiness.

NARCOLEPSY

- Excessive day time sleepiness
- Familial incidence strongly a/w HLA DR-2, and HLA-DQW1 locus on chromosome 6
- Hallmark is ↓ REM latency (REM sleep occurs within 10 minutes of the onset of sleep in place of normal 90 min)
- Classic tetrad is -
 - Sleep attacks (m/c)
 - Cataplexy (sudden loss of voluntary m/s tone but clear consciousness)
 - Hypnagogic hallucinations (occurs at awakening)
 - Sleep paralysis
- * There is ↓ in hypocretin (orexin) producing neurons in hypothalamus
- T/t - forced naps and amphetamines.

Obstructive Sleep Apnea (OSA)

- * M/c cause of excessive day time sleepiness
- Breathing ceases for >10 s during frequent episodes of obstruction of airways (especially pharynx) d/to ↓ m/s tone. There is also a change in the central respiratory drive. Snoring is common.
- * ↓ stage 3 and 4 NREM.

Periodic limb movement disorder (PLMD)

- * Stereotyped rhythmic extension of great toe and dorsiflexion of the ankle and knee during sleep.
- Similar to restless leg syndrome
- EMG : Bursts of activity during 1st hr of NREM
- ↓ stage 3 and 4 NREM but duration of NREM stage 1 may be increased.

Neurotransmitter levels

- Schizophrenia --- ↑ serotonin, nor-adrenaline, dopamine
- Depression --- ↓ serotonin, nor-adrenaline, dopamine
- * OCD --- ↓ serotonin
- * Alzheimer's d/s --- ↓ ACh and nor-adrenaline

- Serotonin is involved in OCD, so serotonin inhibitors (SSRIs) are useful in t/t of OCD.
- ↓ GABA is seen in --- Epilepsy, Anxiety and sleep disorders
- ↓ Glycine is seen in --- Mental retardation, seizures, spastic paraplegia
- ↓ 5-HT & ↓ NA is seen in --- OCD, eating, sleeping, depression.
- * Panic attack is a/w --- Disturbances in serotonin, NA, GABA, dopa, and cholecystokinin.

Ego Defence Mechanisms

- Isolation of affect --- in Obsession
- Reaction formation --- in OCD
- Undoing --- in compulsion
- * Displacement, inhibition --- in phobia
- Repression --- in Anxiety disorder, phobia
- * Dissociation --- in Fugue, multiple personality, somnambulism

IMPORTANT PSYCHIATRIC TESTS

Tests of intelligence

- Wechsler adult intelligence scale
- Stanford-Binet test, (Malin's intelligence scale for Indian children, universal non-verbal intelligence test)

Projective tests for personality

- Rorschach inkblot test
- TAT (Thematic apperception test)
- DAPT (Draw-a-person test)
- * SSCT (sack's sentence completion test), MMPI (Minnesota multiphasic personality inventory)

Neuropsychological tests

- BG Test (Bender Gestalt test)
- BVRT (Benton visual retention test)
- Wisconsin card sorting test
- * Wechsler's memory scale, PGI memory scale
- Luria- Nabraska & Halstead-Reitan test battery, PGI test battery of brain dysfunction (trail making test, stroop test, 'N' back test)

HALLUCINATIONS, DELUSIONS

- **Illusion** --- False (bizarre) perception of external object which has real existence (Disorder of perception). Mis-interpretation of stimulus.
- **Hallucination** --- Disorder of perception. There is false sense of perception in absence of external percept or external stimulus.
- **Delusion** --- Disorder of thoughts (thinking). False, firm (unshakable) beliefs in something which is not a fact & not shared by other people. Belief which is out of keeping with person socio-cultural background & is of morbid origin
- **Impulse** --- Irresistible desire
- * **Obsessions** --- Recurrent, irrational, intrusive, ego-dystonic and ego-alien ideas

HALLUCINATIONS

Hallucination is a false sense of perception without external object or stimulus to produce it. These are independent of will of observer.

- Overall m/c type of hallucinations are --- **Auditory** hallucinations. Seen in alcoholism, schizophrenia, and in functional (hysterical) disorders.
- Hallucinations seen in schizophrenia are --- auditory (m/c), third person hallucination (most characteristic), tactile.
- Visual hallucinations are seen in organic mental disorders
- * Tactile and visual hallucinations (cocaine bugs) with jet black tongue are seen in --- cocaine poisoning.
- * Tactile hallucinations may occur in chronic amphetamine intoxication.
- * Synaesthesia (Reflex hallucination): Stimulus in one modality and hallucination in other modality. E.g. sneezing in front of patient causes headache.
- * Functional hallucination: Both stimulus and hallucination in same modality.
- Pseudo- hallucination & true hallucination:

Pseudo hallucination

- Insight +
- ✓ Subjective
- * Independent of will, involuntary and as real as true perception
- * Sensory organs NOT involved

True hallucination

- Insight +
- ✓ Objective

DELUSIONS

Delusion is a false (firm & unshakable) belief in something which is not a fact

- Delusions are NOT a feature of --- Conversion disorder.
- Fragmentary --- Delirium, hebephrenic schizophrenia
- Of Grandiosity --- Mania
- Of reference, of infidelity of persecution, --- Schizophrenia (esp. paranoid type)

Important Delusion syndromes

Content of Delusion	Syndrome
Jealousy (infidelity) involving spouse	Othello syndrome (or conjugal paranoia)
Erotic, delusion of love	Erotomania or Clerambault's syndrome
Body being ugly	Delusional dysmorphia
Infestations by worms or foreign body	Delusional halitosis (Parasitosis)
Delusion of double (Secret lovers)	Capgras syndrome
Delusion of grandeur, inflated self esteem, and self image	Mania

Induced delusion disorders → sharing of delusions b/w usually two or occasionally more persons.

Nihilistic delusion and delusion of guilt and poverty → Seen in depression.

La belle sign (or La belle indifference) is seen in dissociative disorder.

CHILD PSYCHIATRY

- Concrete thinking stage 2-7 years.
- Abstract/conceptual thinking stage 7-11 years.
- Down's syndrome is most common chromosomal cause and most common cause of severe mental retardation.
- M/c mental disorder in children is Neurosis
- M/c form of pica is Geophagia.
- Termites are mentally gifted children with IQ > 150 (Mens comprises people with IQ > 140)
- Kanner's autistic triad :
Autistic aloofness + Speech / language disorder + Obsessive desire for sameness.
- Fear of death : M/c at the age of 5 years.

* Defiance, oppositionalism and temper tantrums are often used by children 18mth-3yrs of age.

Most children have obtained bladder control during the day & night by the age of 5 year.

* Children starts identifying themselves as boy or girl by ~ 18 month of age (establish a gender identity b/w 18-30 months). By 30 month gender constancy & it is resistant to change.

0-2 yrs --- Actualism to dualism

2-7 yrs --- Animalism

7-16 yrs --- Realism

Older classification of mental retardation

1. Idiots - Mental age of 2 yrs or less

2. Imbeciles - Mental age of 2-7 yrs

3. Morons - Mental age of 7-12 yrs

* Most child psychiatric disorders (e.g. ADHD, conduct, GDT Synd., Tics, Enuresis, autism) are more common in males except mutism (more common in girls).

Dyslexia

Developmental reading disorder. Problems may include omissions, distortions, or substitutions of words, or simply slow reacting.

Dyscalculia

Developmental arithmetic or mathematic disorder

AUTISM

Self occupied, exists in community and pseudo-community.

* Pervasive developmental disorder

* More common in males

Onset is usually < 2 1/2 yrs

C/by

* Marked impairment in reciprocal social and interpersonal interactions

- Marked impairment in language and communications

* Abnormal behaviour

* Mental retardation

* Epilepsy may be seen in idiot savant syndrome. EEG may be abnormal (Epileptiform EEG discharges are seen in 80-85% of patients).

Perinatal CNS insult, raised serotonin levels in etiology

T/t : behaviour therapy; Drugs effective are: fenfluramine, haloperidol.

In Asperger's syndrome language is normal.

Conduct disorder

- * Basic rights of others are violated and rules are not followed.
- Psychological disorder diagnosed in childhood or adolescence that presents itself through a repetitive and persistent pattern of behavior (Anti-social behavior). *
- A/w ADHD.
- T/t seeks to integrate individual, school, and family settings (Multi-Systemic Treatment MST).

Attention Deficit Hyperkinetic Disorder (ADHD)

More common in males, the onset occurs before the age of 7 years. C/ by :

- Poor attention span with distractibility
- Hyperactivity
- Impulsivity

* Moving about here & there

* Talks excessively

Inattention	Hyperactivity	Impulsivity
<ul style="list-style-type: none"> Does not seem to listen when spoken directly Has a difficulty in sustaining in play or tasks Difficulty on organizing talks 	<ul style="list-style-type: none"> * Often leaves seat in class room * Often runs and climbs excessively Has difficulty playing or engaging in leisure activity quietly * Talks excessively 	<ul style="list-style-type: none"> * Has difficulty awaiting turn Interrupts or intrudes on others (disturb in conversation or in games)
<ul style="list-style-type: none"> Does not follow thorough on instructions Forgetful in daily activities 		

MENTAL RETARDATION (MR)

- Classification of mental retardation/ mental handicap/ Intellectual disability

	(Educable)	(Trainable)	(Custodian)	
Borderline	Mild	Moderate	Severe	<u>Profound</u>
90-71	70-50	50-35	35-20	<20

Another terminology

	Moron	Imbecile	Idiot
I.Q.	70-51	50-25	25-0

- Intelligence Quotient (IQ) is calculated by formula

$$IQ = \text{mental age} \times 100 / \text{chronological age}$$
 E.g. a 6 year old child with an IQ of 50 is most likely to perform activity of a 3 year old child like copy a triangle.

* Retinoblastoma, myopia, asthma and high serum uric acid levels are a/w high I.Q. in children.

[Mnemonic - RAMU]

* 3 M/c causes of MR are - Down's syndrome, Fragile-X syndrome & fetal alcohol syndrome.

→ M/c cause of MR overall → Down's syndrome

→ M/c genetic cause of MR → Down's syndrome (Trisomy 21)

* M/c inherited cause of MR → Fragile -X syndrome

THERAPEUTIC

T/t of Choice For

- * Hypochondriasis, somatoform d/s Anxiety neurosis, hysteria --- Supportive Psychotherapy
- Phobia --- Systemic desensitization [Behavior therapy]
- OCD --- 1. Systemic desensitization /exposure and response prevention therapy [Behavior therapy]
 2. Drugs : Clomipramine is gold standard
Fluoxetine and other SSRIs are preferred now a days
- * ADHD --- Methylphenidate
- Gilles de la Tourette's syndrome --- Haloperidol
- * Non-organic encopresis → Behavior therapy
- * For Panic disorder → Imipramine (Escitalopram, paroxetine)
- * For acute panic attacks → Alprazolam
- * Chronic Schizophrenia → Fluphenazine i.v. depot injections

- o Delusional depression --- *Antidepressant*
[Depression with psychotic features] + ECT or antipsychotics [CPZ, Haloperidol, pimozide]
- o Paranoid delusional disorder with somatic / hypochondrial delusion. --- Pimozide
- o Delirium tremens --- Diazepam
- * Resistant cases of schizophrenia
 - A. With +ve symp --- CPZ
 - B. Without +ve symp --- Clozapine
- o Milieu therapy / Therapeutic community / family therapy --- In Schizophrenia
- * Bio feedback, Jacobson's --- In type A behavior / relaxation technique, personality (Psychosomatic disorder)
- o Squeeze technique --- In premature ejaculation (Masters & Johnson's)
- ✓ Abreaction therapy --- In hysteria & d/g of catatonic syndrome.
(Amytal interview) (Interview with mute, stupor)
- o Behavior therapy
 - ✓ Systemic desensitization --- TOC in Phobias OCD
 - ✓ Aversion therapy → Alcohol dependence, transvestism, homosexuality, hysteria
 - * Flooding: --- Phobias

ECT

- o More effective on non-dominant side ✓
- o Premedication with atropine/ glycopyrrolate is required.
- o M/A : ECT produces GTCS lasting at least 25-30 sec. It possibly affects the catecholamines pathway b/w diencephalon and limbic system
- * Dose 110 volts, for 0.6 sec., 1600 M.A. current.
- o Indications
 1. Major severe depression --- A/w suicidal risk, stupor, melancholia, psychotic features
 2. Severe functional catatonia --- A/w ↓ oral intake, stupor, Schizoaffective features
 3. Severe Psychosis --- A/w suicidal risk, no response to antipsychotics. (Schizophrenia/mania)
- * ECT can be given in old age and in pregnancy.
- * ECT is NOT effective in OCD, phobia, personality disorder (neurotic patient).

Ad/E

- Retrograde amnesia is characteristic. Anterograde amnesia is also seen
- # of thoracic spine, femur, humerus (common)
- Headache, bodyache, vomiting, confusion
- * Raised ICT (↓ IOT) (especially with direct ECT)
- o Contraindications
 - Absolute C/I --- Raised ICT
 - Relative C/I --- Recent MI, severe HTN & severe pulmonary disease, pheochromocytoma
- ✓ *Amnesia (memory loss) is common ad/e after modified ECT which recovers in few week*
- ✓ *Bodyache / headache is common after Direct / unmodified ECT.*
- ✓ *ECT is not or least effective in chronic schizophrenia.*
- * *Major severe depression with suicidal risk is the most important indication for ECT.*
- *In mania & schizophrenia used of ECT is reserved only for above-mentioned indication.*

LITHIUM

- o DOC in ✓
 - T/t of acute manic episode in a patient of bipolar disorder is the m/c indication
 - MDP (bipolar disorders)
 - Acute mania,
 - Prophylaxis of bipolar MDP.
 - Cyclothymia
- o Prophylactic dose of Li in BPD → 0.6 - 0.8 meq/ L
- o Prophylactic maintenance level is 0.5 - 0.8 meq/ L
- ✓ Normal therapeutic level is 0.7-1.1 meq/ L. Serum level has to be monitored for patient on lithium therapy.
- * Can cause renal failure. Dialysis should be done at a level > 4 meq/ L. Dialysis is the most effective means of removing Li from body.
- o No specific antidote is available.
- ✓ Other uses of Li are → Graves' d/s, migraine
- o Teratogenic: Can cause Ebstein's anomaly
- * Li should not be used in children < 12 years
- o Ad/e :
 - Tremors (of 4-8 Hz frequency) are m/c side effects which may require dose reduction or propranolol should be added
 - Polyuria (diabetes insipidus), hypothyroidism, nausea, vomiting
 - ✓ Renal failure (Only on long term therapy)
 - ✓ Exacerbation of psoriasis

• AMISULPRIDE
• SERTINDOLE
• ZOTEPINE

CLOZAPINE

- * Most effective antipsychotic.
- Antisuioidal anti-psychotic.
- Atypical antipsychotic which blocks 5-HT₂, D₂>D₁, D₄, M, and α receptors.
- Usual plasma concentration required is 300-600 ng/mL.
- Higher plasma concentration is a/w risk of seizures.
- Causes agranulocytosis in 1-2% of cases.
- * Other ad/e: wt gain, sialorrhoea, sedation, hypotension, DM, seizures (sweating).

Tricyclic Anti Depressants :

Category	Examples
◦ SNRI	Doxepin, Venlafaxine, Trimipramine, Imipramine, Sibutramine, Amitriptyline, Dothiepin [DVT in DAS]
◦ NRI (NA>5TH)	Maprotiline, Amoxapine, Nortriptyline, Desipramine [MAND]
◦ SSRI	Fluoxetine, Fluvoxamine, Paroxetine [FFP]
◦ SSR Enhancer	Tianeptin, Mianserin
◦ Atypical	Trazodone, bupripion

* Atomoxetine is a newer SNRI drug approved for the treatment of ADHD.

* Aripazole is an antipsychotic with least sedative side effect.

* Risperidone is 2nd generation antipsychotic.

Ad/E of Anti-psychotics, anti-depressants

Act on cortex and mesolimbic system

Ad/E:	Max ^m	Min ^m
◦ Autonomic (α-blockade)	CPZ, Triflupromazine	Haloperidol
◦ EPS	Haloperidol (++++) Fluphenazine (++++)	Thioridazine (+) Clozapine (nil)
◦ Anti-cholinergic (Among Anti-psychotics)	Thioridazine	Haloperidol/ Trifluoperazine
◦ Anti-cholinergic (Among Anti-depressants)	Amitriptyline	Fluoxetine, Trazodone
◦ Agranulocytosis	Clozapine	Haloperidol

SDRB drugs

- ✓ Antipsychotic which blocks 5-HT, Dopamine receptors.
- Examples: Amisulpride, sertindole, zotepine.
- EPS are not seen with clozapine
- ✓ Clozapine is particularly effective in resistant schizophrenia.
- Akathisia is m/c with haloperidol. Treated by propranolol.
- * DOC for haloperidol/ neuroleptics induced akathisia --- Beta blocker.
- * Antidepressant which can be used in t/t of nocturnal enuresis, ADHD, and chronic pain --- Imipramine

EATING DISORDERS

Eating Disorders

Features	Anorexia Nervosa	Bulimia Nervosa
◦ Age group	Adolescent females	Early teens
◦ Body image	Disturbed	Disturbed
◦ Cl/f	Refusal to maintain body weight above normal	Irresistible craving for food with episodes of over eating
◦ Diet	Very less eating	Binge eating is f/b * Self induced vomiting * Periods of starvation * Use of purgatives and appetite suppressants
◦ Weight	Underweight (85%)	Normal (100%)
◦ Amenorrhoea	100%	50%
◦ T/t	Behaviour therapy	Fluoxetine

- * Patients of anorexia nervosa are vulnerable to sudden death from ventricular tachyarrhythmias

PSYCHIATRIC DISORDERS

- In ICD-10 classification mental illnesses/disorders are given in chapter 5.
- M/c psychiatric disorder a/w DALY (Disability Adjusted Life Year) loss of work is schizophrenia.

- Primary psychiatric causes of psychosis include the following:
 - Schizophrenia & schizophreniform disorder
 - Affective (mood) disorders, including severe depression, and severe depression or mania in bipolar disorder (manic depression). People experiencing a psychotic episode in the context of depression may experience persecutory or self-blaming delusions or hallucinations, while people experiencing a psychotic episode in the context of mania may form grandiose delusions.
 - Schizoaffective disorder, involving symptoms of both schizophrenia and mood disorders
 - Brief psychotic d/o, or acute/transient psychotic disorder
 - Delusional disorder (persistent delusional disorder)
 - Chronic hallucinatory psychosis.

Psychosis & Neurosis can be differentiated by

Psychosis	Neurosis
<ol style="list-style-type: none"> Loss of / Gross impairment of <ul style="list-style-type: none"> Judgment / reality testing Affects, thoughts Insight Personality disturbances seen Organic symptoms like delusions and hallucinations are common A/w severe changes in affect, <u>thoughts</u> E.g. schizophrenia, mania, psychotic depression 	<ol style="list-style-type: none"> Preserved/ least effect on <ul style="list-style-type: none"> Judgment / contact with reality Affects, thoughts Insight Personality preserved. —nt Neither a/w severe changes in affect nor with change in thoughts E.g. panic, phobia, OCD

Old Classification (WHO 1965)

Psychosis		Neurosis
Organic Psychoses	Non-organic / functional	
<ul style="list-style-type: none"> Drug induced psychoses Delirium Presenile / Senile dementia * Organic amnestic syndrome * Drug induced psychoses Intracranial infections induced 	<ul style="list-style-type: none"> Delusional disorder Schizophrenia Schizo-affective disorders Acute psychosis Mood disorders <ul style="list-style-type: none"> Mania, Depression 	<ul style="list-style-type: none"> Phobias Panic disorders Anxiety disorders Dissociative / conversion disorder OCD Somatoform disorders Personality disorders

✚ Delirium is m/c organic disorder.

* Drugs inducing psychosis are --- Alcohol, heroin, morphine, cannabis, cocaine, LSD etc.

✚ Psychosis may occur in pregnancy, postpartum, epilepsy.

* Disorientation may occur in - acute organic brain syndrome (Delirium).

- Psychiatric triangle has 3 component

Affect - Feeling
Cognition - Thought
Conation - Action

- Cognition (thought) Disorders are

Delusion, OCN, Phobias, Schizophrenia

Thought has 4 components:

- Form (How things are connected to each other, association)
- Flow
- Possession (My own thoughts are under my control)
- Content

Thought Disorder

Thought Component	Alteration in content	Seen in
1. Form	Loss of association	Schizophrenia
	Verbigeration (senseless repetition)	Schizophrenia
2. Flow	✓ Flight of ideas (↑ flow), Clang association	Mania
	Thought retardation (↓ flow)	Depression
3. Possession	Thoughts are my own but not under my control	OCD
	Not my own thoughts, not under my control ✓ (Thought alienation)	Schizophrenia
4 Content	Change in content	Delusion

- Cognitive theory

Based on psychotherapy given by (T. Beck) A/c to cognitive theory specific cognitive distortions in few patients make them prone to develop specific mental illnesses. These are referred to as automatic thoughts or cognitive errors. Modifications of these cognitive errors is a standard approach in (behaviour therapy). Examples of cognitive errors are ---

✓ Overgeneralising, selective abstraction, excessive responsibility, assuming temporal causality, self references, catastrophizing, dichotomous thinking.

- * Inhibited grief : Denial of loss ✓
- ✓ Anniversary reaction : Grief reaction on death anniversary.

Duration Criterias to define Psychiatric illnesses:

Disorder	Minimum Duration
Hypomania	4 days
Mania	7 days
* Major Depression	→ 2 wks +
* OCD	→ 2 wks
Acute psychosis	<1 month
Acute delusional psychoses	<3 month
Schizophreniform disorder	<6 month
Schizophrenia	>6 months
Generalised anxiety disorders	6 months
Chronic Grief	>6 months
Dysthymia/ Cyclothymia	>2 yrs
Inhibited Grief	Denial of loss

- Adjustment disorder : symptoms should start within 3 months and should not last >6 months. Always accompanied by stress. (while stress is NOT required in depression).
- Adjustment disorder with prolonged depression may last upto 2 yr.

Wernicke's Koraskoff encephalopathy/ Amnestic Syndromes

	Wernicke's encephalopathy	Koraskoff's Psychosis
* M/c cause	Alcoholism	✓ Prolonged alcoholism
* Triad of	Nystagmus + LR palsy (External ophthalmoplegia) + Ataxia + Amnesia	Confabulation + Amnesia +
* Higher functions	Disturbed	Retained (Patient is alert, conscious, intellect ⁺)
◦ M/c site	Diffuse involvement	Mammillary bodies of hippocampus
◦ Other features	✓ Acute delirium like state pupillary reflex normal	Abstract thinking *

- ✓ In Koraskoff's psychoses Immediate & remote memory is usually retained

Delirium & Dementia

	Delirium (Acute confusional state)	Dementia	Organic Amnestic syndrome
◦ Consciousness	↓ (Clouding)	N	N
* Attention	↓↓	N	N
✓ Orientation esp. of time	Grossly disturbed	N/↓	N
◦ Behavior	Impaired	Impaired	
◦ Memory impairment			
* Immediate	↓	N	N
* Recent	↓	↓	↓↓
- Remote/past	N	N or late impairment	↓
- Vigilance	↑		

- In late phase profound anterograde amnesia & milder retrograde amnesia is found

- * In acute delirium sun downing is present i.e. worsening of symptoms in the evening and night

- Cortical dementia is seen in head injury. Dx of dementia requires 6 months except in head injury.
- Sub-cortical dementia is seen in Huntington's chorea, parkinson's d/s, Wilson's d/s, progressive supranuclear palsy, and AIDS while cortical dementia is seen in Alzheimer's d/s and Pick's d/s
- Hypothyroidism is m/c reversible and treatable cause of dementia.
- Dementia pugilistica (Punch drunk syndrome) is seen in boxers. D/to repeated minor trauma to brain.
- Dementia praecox psychoses with no memory loss. Loss of personality d/to delusions or hallucinations.

Amnesia:

- Anterograde amnesia (Inability to restore recent memory)
 1. Also called post traumatic amnesia
 2. Two types
 - * Drug induced : BZD
 - * Post traumatic : usually follows head injury
 3. Can be seen after shock, or following emotional disorder, stroke, Alzheimer's d/s.
 4. New events are not transferred into long term memory.

- **Retrograde amnesia** (Inability to restore recent memory)
 1. Loss of memory for events preceding the onset of the amnesia.
 2. Seen in diencephalic amnesic syndromes.
(Korsakoff's syndrome.)

SUICIDE

- * Depression is the m/c cause of suicide in psychiatric patient.
- People with a diagnosis of a personality disorder, particularly borderline, antisocial or narcissistic personality disorders, are at a high risk of suicide
- Suicide risk in psychiatric patient:-

Psychiatric disorder	Risk %	↑ed risk from general population
✓ Major depression	15%	30 fold ↑
✓ Schizophrenia	10-13%	
Bipolar disorder →		15 fold ↑
Anorexia nervosa		40 fold ↑
Mood disorder	1%	

SCHIZOPHRENIA

Eugen Bleuler's fundamental symptoms (4A's)

- * Ambivalence (double mindness/ confusion)
- Autism (withdrawal into self)
- Affect disturbances
- Association loss

Schneider's first rank symptoms

- Hallucinations (3rd person, voices commenting on one's action)
- Thought alienation (Thought -withdrawal/ -insertion/ -diffusion/ broadcasting)
- * Passivity phenomena (Made -feeling/ -impulse/ -volitions or acts; somatic passivity)
- Delusional perception, thought echo

Criteria for D/g:

Presence of ≥2 features for >6 months (DSM criteria)

- Delusion
- Hallucinations
- Disorganised speech
- Grossly disorganised or catatonic behaviour
- Negative symptoms (affective flattening or blunting)

Retarded or stuporous Catatonia

- C/by extreme psychomotor retardation (severe form) of catatonic schizophrenia
- (Mutism, rigidity, posturing, stupor, negativism, echopraxia, waxy flexibility, ambitendency are seen)

Other findings seen in schizophrenia

- Anhedonia** --- Inability to experience pleasure (also seen in PTSD / post traumatic stress disorder)
- Avolition** --- lack of initiative.
- Apathy** --- lack of feeling or emotions.
- * **Perservation** --- Persistent (or) inappropriate repetition of same thoughts
- * **Verbegeration** --- Senseless repetition of same words beyond their relevance. Part of formal thought disorder.

→ Amotivation is lethargy, apathy, loss of interest, anergia, reduced drive and lack of ambition. Seen in chronic cannabis abuse

→ Depersonalization & derealization usually occur together and are seen in --- depression, anxiety, schizophrenia, epilepsy etc.

✓ Pseudo-community is seen in --- schizophrenia

✓ Split personality is seen in --- schizophrenia

* Morbid jealousy is seen in --- Mood disorder, Alcoholism, Drug abuse, Epilepsy, Schizophrenia (MADES)

Subtypes

	P/g	Onset	Delusions	C/F
Catatonic	Best	Late	<u>Negativism</u>	<ul style="list-style-type: none"> ✓ <u>Marked disturbance (cata)</u> ✓ <u>in motor behaviour (tonic)</u> Verbal ejaculations <u>echopraxia,</u> <u>echolalia</u> <u>verbegerations.</u> Automatic obedience Ambitendency Stupor, <u>mutism,</u> <u>Waxy flexibility,</u> Rigidity & posturing
Paranoid (M/c form)		Late	<ul style="list-style-type: none"> Persecution, Reference, Jealousy, <u>Grandiosity</u> 	<ul style="list-style-type: none"> Much less personality changes, <u>c/b induced by amphetamines,</u> <u>Somatic passivity</u>
Hebephrenic (Disorganized)	Worst	Early	<ul style="list-style-type: none"> Fragmentary (changing) delusions / hallucinations 	<ul style="list-style-type: none"> Highly disorganized thoughts, ✓ <u>Neologism</u> ✓ <u>Crimacing</u> ✓ <u>Mannerism</u> (Mirror gazing) Mixed behaviour
Un-differentiated			Fragmented & un-systematized	

- Catatonic -- Best p/g (best response to ECT), late onset
- Paranoid -- Most common form, late onset
- Hebephrenic -- Worst p/g, early onset
- * Simple -- least common, early onset worse prognosis

Good prognostic factors for schizophrenia

- o Onset : Acute or abrupt, after 35 yrs,
- o Presence of : precipitants/ stressors, depression, positive symptoms
- o Catatonic subtype
- o First episode, female sex,
- o CT : normal

→ Family history, past history, negative symptoms, male with asthetic physique, hospitalization, poor drug response are a/w poor p/g.

* Suicide is the most important factor for premature mortality in schizophrenia. The most imp. factor for suicide is presence of a major depressive episode.

MOOD DISORDERS

Mood disorders are type of psychoses.

Mania

- o Absence of an underlying organic cause
- * Sleep is usually reduced with a ↓ed need for sleep
- * Delusion of persecution may be seen.
- o 4 stages are seen

1. Elevated Mood

- * Euphoria
 - Elation of mood
 - Exaltation
- ✓ Ecstasy (very severe elevation)
- * Expansive mood

2. Psychomotor activity

- * Overactivity restlessness
- * Sometimes in "stuporous state (manic stupor)"

3. Goal directed activity

- * Unusually overalert
- * Hypersexual and promiscuous
 - ↑ sociability
- * Distributing money

4. Speech & thought

- More talkative
- Pressure of speech
- * Delusion of grandiosity

* Dis-inhibition+

✓ There is flight of ideas (Subsequent thought follow rapidly, connection is by chance) → clang association.

Bipolar disorders

- o Also k/as bipolar affective disorder, historically k/as manic-depressive disorder.
- o Bipolar disorder is a psychiatric diagnosis that describes a category of mood disorders defined by the presence of one or more episodes of abnormally elevated energy levels, cognition, and mood with or without one or more depressive episodes.
- o The elevated moods are clinically referred to as mania or, if milder, hypomania.
- o T/t of BPD :
 - ① Manic phase (Acute manic episode) → Li is DOC.
 - ② Depressive phase → Lamotrigene & Li
 - ③ Rapid cyclers → Carbamazepine is DOC, valproate is also useful.
- * Li is used for prophylaxis & t/t of manic episode.

The disorder has been subdivided into:

- o Bipolar type I :
C/by clinical course of ≥1 manic episode and sometimes major depressive episode.
- o Bipolar type II :
C/by episodes of major depression + hypomania. Hospitalization is not required.
- * Cyclothymia :
Type of chronic mood disorder widely considered to be a milder or subthreshold form of bipolar disorder .

DEPRESSION

- o Common in middle aged females
- * Most important feature is sadness or loss of interest in all activities (depressive mood)
- o Other characteristic features are ---
Early morning awakening, ↓ appetite and weight, psychomotor agitation or retardation, loss of sexual drive
- o In severe depression there may be anhedonia (inability to experience pleasure)
- ✓ Suicidal ideas (risk more in males >40 years, unmarried/ divorced/ widowed, early stage, recovery phase, marked hopelessness)
- * Social withdrawal+
- * Delusion of nihilism
- ✓ Severe depressive episode is a/w --- OCD post partum psychosis, AIDS, cancer, post MI
- * Drugs causing depression -- Steroids (m/c),

- * ↓ serotonin, ↓ NE levels are found
- Latest t/t modalities for resistant depression
 - TMS (Transcranial magnetic stimulation)
 - VNS (Vagus nerve stimulation)
 - DBS (deep brain stimulation)

Dysthymia is any mild depression which is serious enough to be called depressive episode and lasts for ≥ 2 yrs.

NEUROTIC DISORDERS / NEUROSES

- ✓ Anxiety is commonest psychiatric symptom & Generalised anxiety disorders are m/c psychiatric disorder in general population.
- Depression is the commonest psychiatric disorder in hospitalized patients
- ✓ Depression is the m/c psychiatric disorder in Hypothyroidism, AIDS, patient on OCP, post partum psychosis

Obsessive compulsive Disorders (OCD)

- * Disorder of thought (cognition)
 - An obsession is an idea, impulse or image which intrudes into conscious awareness repeatedly
 - It is one's own idea/impulse but is ego-alien (foreign to one's personality)
 - Age of onset late 20s
 - Depression is commonly associated
- * Washers are m/c type
 - Defense mechanism which are involved – isolation of affect, undoing (Patient attempts to ignore or suppress but he is unable to do so)
- ✓ Serotonin is biochemical mediator
 - T/t of OCD
 - * Behaviour therapy is TOC

In this thought stopping, response prevention, systematic desensitization and modeling are used
 - Drugs
 - * Clomipramine (a non-specific SRI) is the gold standard.

Fluoxetine and other SSRIs (sertraline, citalopram etc.) are preferred now a days

Other drugs which are useful- Antipsychotics (like haloperidol), Buspirone
 - * ECT is indicated when there is suicidal risk or poor response to drugs/ behaviour therapy

General adaptation syndrome (GAS)

- Term used to describe the body's short-term and long-term reactions to stress.

- * Stressors in humans include such physical stressors as starvation, being hit by a car, or suffering through severe weather. Additionally, humans can suffer such emotional or mental stressors as the loss of a loved one, the inability to solve a problem, or even having a difficult day at work.
- Stages:
 - Alarm reaction (AR),
 - Stage of resistance (SR), and the
 - Stage of exhaustion (SE)

Types of personality

	C/F	↑ Risk of
1. Type A	Achievement oriented people, often high-achieving "workaholics"	Coronary heart diseases
2. Type B	Easy going relaxed individuals	-
3. Type D	Distressed	CHD patient has ↑ Mortality & recurrence from MI

Personality disorders

Emotionally unstable personality disorder

- * Marked tendency to act impulsively without consideration of consequences
- * Emotional instability (frequent mood swings) is essentially present
- Two types
 1. Impulsive type is c/by outbursts of violence or threatening behaviour (in response to criticism by others)
 2. Borderline type is c/by disturbed own image and internal/sexual preferences. Unstable and intense inter personal relationships. Tendency of deliberate self-harm, self mutilation, suicidal gestures are characteristic
- * This type of personality is seen in ambulatory schizophrenia and pseudoneurotic schizophrenia
 - Ambulatory schizophrenia and pseudoneurotic schizophrenia are now included in Borderline personality disorder
- ✓ Splitting is a defense mechanism against BPD

Anti-social personality disorder

- There is disregard for social norms, rules and obligations. Very low tolerance to frustration and a low threshold for discharge of aggression
- More common in males
- Sometimes similar to 'psychopath' or 'sociopath'

Disorders D/to Reaction to stress/ adjustment Post traumatic stress disorder (PTSD)

- Seen in females after serious accidents/ rape/ disaster/ war. Person try to avoid events or stimulus that arouse memory recall of the stressful event

- Symptoms develop after a period of latency (≥ 6 months)
- * Symptoms are recurrent flashbacks/ dreams of event, fear, marked anxiety making arousals in night.
- Partial amnesia and anhedonia may be seen

Adjustment disorder

- Seen in adolescent females
- Presents with marked distress, depressed mood, anxiety, disturbed conduct, emotions and suicidal attempts
- Maladaptive response to stressful life event. Usually seen within 1 month of stressor or significant change in life (e.g. to place an adolescent in boarding school against her interest)

Dissociative Disorders

Dissociative Amnesia

- Commonest type of dissociative disorder. Occurs in adolescent and young adults (F>M)
- Sudden inability to recall important personal information (Amnesia), particularly concerning stressful or traumatic life events Patient is aware of amnesia
- There may be clouding of consciousness
- Physical examination and investigations are normal

Dissociative fugue:

- * Episodes of wandering away (usually from home). During episode, person usually adopts a new identity with complete amnesia for earlier life. Patient is unaware of amnesia
- Onset is sudden & termination is too abrupt.

Ganser's Syndrome

- Hysterical pseudodementia commonly found in prison inmates
- Characteristic feature is vorbereiten which is also called as "approximate answer"
- * Characterised by approximate answers, hallucinations clouding of consciousness & psychogenic physical symptoms.

La-belle-indifference is a clinical feature of dissociative disorder. There is lack of concern towards symptoms, despite the apparent severity of disability produced. Earlier thought to be hallmark of dissociative disorder, but now known to be present even in physical illness.

Munchausen Syndrome

(Factitious disorder / hospital addiction)

- * Patient who repeatedly simulate or fake diseases for the sole purpose of obtaining medical attention

- No motive

Phobic disorders or phobia

- ✓ In phobias insight is present.
- * In phobia primary defense mechanism is repression and secondary defense mechanism is displacement
- Agoraphobia is commonest type of phobia char/by irrational fear of being in unfamiliar places (crowd/public places / open space) from where it is not easy escape to a safe place (e.f. a lift).
- Claustrophobia is fear of closed spaces e.g. fear of MRI machine
- Social phobias – Irrational fear of activities or social interactions, Erythrophobia (fear of blushing), shy bladder (fear of urinating in public lavatory).
- ✓ Acrophobia (fear of high places)
- Xenophobia (fear of strangers)
- * Behaviour therapy (esp. systemic desensitization) is TOC. Among drugs alprazolam (BZD's) is DOC.
- ** SD is based on reciprocal inhibition (Wolfe principle) & consists of 3 main steps. **
 - Relaxation training
 - Hierarchy construction
 - Systematic desensitization proper.
- ✓ Relaxation training include Jacobson's progressive muscular relaxation, hypnosis, yoga, shavasna, biofeedback, yoga nindra, pranayama, vipasna.
- ✓ Relaxation techniques are also an integral part of majority of behaviour therapy

Panic Attack

- * Is a period of intense fear developing instantly which peaking within 10 min.
- E.g. fear just before appearing in exam.

SOMATOFORM DISORDERS

- Somatization disorder
- Conversion disorder
- Hypochondriasis
- Factitious disorder
- Somatoform pain disorders

There is no organic basis/pathology behind these disorders.

Psycho-somatic disorders

- Bronchial asthma
- UC
- RA
- ✓ Peptic ulcer
- ✓ Essential hypertension
- ✓ Neurodermatitis

[PEO Nescafe BRU]

SEXUAL DISORDERS

Erectile dysfunction

- * Inability to have or sustain penile erection till the completion of satisfactory sexual activity.
- * Early morning erections and nocturnal penile tumescence are usually preserved (they are lost in organic impotence)

Premature ejaculation

- Performance anxiety is the m/c cause of it.
- Seman's squeeze technique is used in t/t.

- ✓ Sensate focus technique is used for t/t of impotence
- * Master's and Johnson's technique is "most popular t/t method for psychosexual dysfunction. In this both the partners are treated together (dual sex therapy)
- Excessive sexual drive is called satyriasm in men and nymphomania in women.

Fetishism

- * Sexual arousal occurs mainly with a non-living object
- ✓ Fetish object may include clothes of opposite sex

Frotteurism

- Persistent or recurrent involvement in the act of touching or rubbing against an unsuspected person of opposite sex
- Frottage is often employed in crowded places like buses. Often seen in adolescent males

Erotomania

- Type of delusion in which the affected person believes that another person, usually a stranger, high-status or famous person, is in love with him

"JELLINEK"

SUBSTANCE ABUSE

ALCOHOLISM

- Acc/to Jellinek alcoholism c/b classified into 5 subtypes on the basis of pattern of use. $\alpha, \beta, \gamma, \delta, \epsilon$.
- * Gamma alcoholism is called malignant alcoholism
- * Dipsomania (compulsive drinking) is seen in epsilon alcoholism
- * "CAGE questionnaire", AUDIT and MAST are used to identify problem drinkers
- In acute intoxication
 - Sensorium changes (in form of excitement) starts at 25-100 mg % BAC (blood alcohol concentration)
 - Level is dangerous if 200-300 mg % BAC
 - Death may occur if > 400 mg % BAC

Alcohol withdrawal

- M/c withdrawal syndrome is hangover next morning (c/ by mild tremors, nausea, vomiting, insomnia, anxiety, and irritability)
- Severe withdrawal can lead to
 - ① Acute tremulousness : m/c symptom
 - ② Delirium Tremens (DT)
 - Acute organic brain syndrome
 - Most severe form of alcohol withdrawal syndrome, occurs after 2-4 days of abstinence
 - C/ by clouding of consciousness, disorientation in time and place, poor attention span, transient "visual" (and sometimes auditory) hallucinations, illusions. Marked autonomic disturbances like fever, sweating, tachycardia, HTN, "pupillary dilation", agitation, insomnia
 2. Rum fits: Tonic clonic seizures.
 3. Alcoholic hallucinosis: C/ by presence of hallucinations usually auditory during abstinence following regular alcohol intake.

- ✓ DOC for withdrawal syndrome is BZD's esp. chlordiazepoxide. Diazepam, carbamazepine is also useful. Thiamine (Vitamin B1) is given for t/t

- ✓ Visual hallucinations are characteristic of alcohol withdrawal.

Complications of alcoholism

(a) Wernicke's Encephalopathy

- Acute reaction to severe thiamine deficiency Ch/ by triad of -

Ophthalmoplegia with B/L external rectus palsy + Ataxia + Global confusion

* Recent memory disturbances

- Peripheral neuropathy and poor attention span

(b) Korsakoff's psychosis:

- Chronic c/c of thiamine deficiency.
- Presents as Amnesic syndrome & char / by Gross memory disturbances with confabulations + amnesia + but insight is often impaired **
- B/L dorsomedial nuclei of thalamus and mamillary bodies lesion is seen.

(c) Marchiafava Bignami disease:

Alcohol related nutritional deficiency.

* If autonomic symptoms with tremors seen -- it is DT

- If confusion + ophthalmoplegia + ataxia seen --- Wernicke's encephalopathy.
- If confabulation with loss of insight then --- Korsakoff's psychosis

Opioid abuse

- Opium is obtained from dried exudate of papaver somniferum
- Most important dependence producing derivatives are morphine and heroin.
- Acute intoxication is char/ by "depression of CVS" (bradycardia, hypotension), respiratory depression, subnormal temperature and pinpoint pupils (remember with the funda that everything decreases in intoxication (i.e. CVS, respiration, temp, pupil size, reflexes etc. and ↑ in opioid withdrawal)
- Opioid withdrawal symptoms
Occur within 12-24 hours. Symptoms and signs are opposite of that of intoxication i.e. ↑ secretions from all orifices like lacrimation, sneezing, rhinorrhoea, vomiting, sweating, diarrhoea, tachycardia, yawning, mydriasis, piloerection, dysphoria, nausea, vomiting etc.

• T/t of opioid dependence

1. T/t of overdose

By antagonists (naloxone is DOC; nalmefene, nalorphine are other useful drugs)

- Naltrexone is used as anticraving agent (to prevent relapse)

2. M/m of withdrawal symptoms

DOC for opioid withdrawal is methadone, clonidine also useful. Methadone has been used primarily as a substitution therapy (detoxification) of opioid dependence. Clonidine is non-opioid drug useful for opioid detoxification.

3. Maintenance phase -- when detoxification phase is over patient is maintained on agonist methadone (most widely used), buprenorphine or on antagonists (nalorphine/naloxone).

4. Prophylaxis -- "Naltrexone c/b" used.

- There is ↑ risk of acute MI in drug abuse d/to intake of Cocaine.
- Cocaine & cannabis can produce delusion of persecution or tactile hallucinosis (Psychoses).
- Dopamine is also responsible for psychosis.
- Fatal dose of nicotine is 30-60 mg.
- Methadone can treat, reverse cocaine addiction.

30-60 mg

• Derivatives of Cannabis:

- Dry leaves → Bhang
- Female plant flower top → Ganza
- Resin exudate from stem/leaves → Charas/Hashish

OVERDOSE SYNDROMES

Serotonin syndrome

- Also k/as "serotonin storm" or hyperserotonemia
- Consequence of excessive serotonergic activity in the CNS and in the PNS.
- C/by- Agitation, diarrhoea, hypertension, hyperreflexia, myoclonus, hyperthermia, ANS instability, seizures, delirium and coma.
- BZD's may help in reducing anxiety. Cyproheptidine is considered DOC which is antagonistic at serotonergic receptors.

Anticholinergic syndrome

* D/to overdose of anti-cholinergic drugs.

- C/by- Bradycardia, blurred vision (mydriasis), constipation, dry mouth, dry skin, epigastric discomfort, urinary retention (esp. in BPH patients)
- BZD's may help in reducing anxiety.

- Alleviate cognitive symptoms
- Acute anticholinergic syndrome is completely reversible and subsides once all of the toxin has been excreted. Previously, reversible cholinergic agents such as physostigmine were used but this was found to increase the risk of cardiac toxicity. The current recommended treatment is symptomatic and supportive management. Piracetam, α -GPC and choline (and other racetams) alleviate cognitive symptoms caused by extended use of anticholinergic drugs.

Tolerance

- Reverse tolerance (sensitization) is a cause of psychosis in cocaine addicts.
- Cross tolerance: ↓ in response to one drug d/to exposure to another drug (t/t with antivirals, antibiotics, analgesics and many other medications). Users with a high tolerance to the stimulant amphetamine may also exhibit a high tolerance to the structurally similar methamphetamine or other amphetamine-like stimulants. The phenomenon is also observed in cigarette smokers, in whom there is a demonstrably lessened sensitivity to the effects of caffeine. Cross-tolerance is also frequent in response to use of hallucinogens (e.g., LSD).

Drug Dependence

	Psychological	Physical
C/F	Inability to stop craving, taking substance at the cost of social life	Tolerance, withdrawal
Seen with	Cocaine, amphetamine, cannabis, LSD, volatile substances & (Tobacco, alcohol, smoking, BZD also)	Tobacco, alcohol, smoking, BZD

- Gateway substances:
Tobacco, alcohol, volatile substances
- Amphetamines (Appetite suppressants) are used to produce model psychoses resembling paranoid schizophrenia in experimental animals. (Cocaine and LSD also useful)
- Drugs producing schizophrenia like state ---
Amphetamines, phencyclidine, cocaine and LSD
- Anabolic steroids produces mania and their withdrawal produces depression.
While glucocorticoids and ACTH are known to produce depression
- Angel dust is phencyclidine. It produces acute schizophrenic reaction (catatonia syndrome) and dissociate anesthesia.
- Rave drugs: Ecstasy or MDMA is a Rave drug which produces euphoria.

SOME POINTS OF SPECIAL MENTION

- Insomnia is seen in --- Alcohol withdrawal.
- Hypersomnia is seen in --- Cocaine withdrawal.
- Kubler Ross classified 5 stages of death: denial → anger → bargain → despair → acceptance.
- Sigmon Freud died in 1939 in London.

Structural model of Mind

1. Instinct : Instinctual drive (ID)

- Inborn
- Based on principle of pleasure
- Maternal/ paternal instincts c/b seen

2. Ego : Based on principle of reality (practical thinking)

3. Super ego : Based on moral principle . Ego ideal. E.g. Mother Teresa, Mahatma Gandhi (Idealistic thing)

Topographical model of Mind

1. Conscious :

2. Unconscious :

- Dream analysis
- Psychoanalysis

3. Preconscious:

Defense mechanism

- Part of ego
- Involuntary automatic unconsciously instigated to keep away unacceptable urges and impulses from conscious
- Types:

Primary : Repression

1. Transference;

D/to past experience affect the current life

2. Counter transference;

Treating the patient as per his/her own experience.

Mature :

- Humour
- Suppression (waiting for the right time)
- Sublimation (Express wrong things in acceptable way)
- Altruism (To do something for other)
- Anticipation

Immature :

- Displacement : for phobia
- Rationalisation: (giving some other explanation)

3. Dissociation

Seen in fugac, MPD (identify), depersonalization, amnesia [FIDA]

Psychotic/ narcissistic defense :

1. Projection :
2. Denial:
3. Distortion/regression

SOME IMP. NEGATIVE POINTS

- Bleuler 4 'A's in Schizophrenia does NOT includes --- Automatism & auditory hallucination
- * Dementia is NOT seen in --- Schizophrenia
- * NOT true about paranoid schizophrenia --- Rapid deterioration of personality
- NOT seen in schizophrenia --- Intellectual impairment
- Hallucinations are NOT seen in --- Personality disorders, anxiety
- * Delusion is NOT seen in --- Compulsive disorder
- Delusions are NOT a feature of --- Conversion disorder.
- NOT a defense mechanism --- Transference, derailment
- Physical withdrawal symptoms are NOT commonly seen with --- **LSD**, Cannabis
- NOT an indication for use of lithium --- Generalised anxiety disorder.
- * NOT a serotonin dopaminergic receptor blocker --- Doxepin.
- NOT an adverse effect of clozapine --- Hypertension
- Drug NOT used in alcohol intoxication --- Acamprosil
- * Behaviour enhancement does NOT include --- Consolidation stage
- Cognitive Behaviour therapy (CBT) does NOT include --- Interpretation.
- * Drug NOT useful in heroin dependence --- Disulfiram
- NOT a feature of delirium tremens --- Oculomotor nerve palsy.
- * NOT a somatoform disorder --- Fibromyalgia.
- * Panic attack is NOT a/w disturbances of which NT - Glutamate.

CLINICAL VIGNETTES

- A patient suffering from pneumonia for 5 days is admitted to the hospital. He suddenly ceases to recognize the treating doctors and staff, thinks that he is in jail and complains of scorpions attacking him. He is in altered sensorium. Most

likely diagnosis is --- acute delirium

Explanation

Patient in the question is suffering from acute confusional disorder acute delirium. He has disturbed consciousness (altered sensorium), disturbed orientation of place (thinks he is in jail), and didn't recognize the doctors and staff so his perception is disturbed (complains of scorpions attacking him)

- Basanti 27 years old female thinks her nose is ugly. Her idea is fixed and not shared by any one else. Whenever she goes out of home, she hides her face with a cloth. Most likely diagnosis is

- A. Delusional disorder (delusional dysmorphia)
- B. Schizophrenia
- C. Hypochondriasis
- D. Personality disorder

Ans.: A. Delusional disorder (delusional dysmorphia)

Delusional disorders are c/by fixed ideas about self/ others. For diagnosis of schizophrenia certain criteria are required.

- A 50 year old male present with a 3 year history of irritability, low mood, lack of interest in surroundings and general dissatisfaction with everything. There is no significant disruption in his sleep or appetite. He is likely to be suffering from : [AIIMS may'07]

- A. Major depression.
 - B. No psychiatric disorder.
 - C. Dysthymia.
 - D. Chronic fatigue syndrome.
- (Ans.: C. Dysthymia)

- **Dysthymia** is defined as any mild depression which is serious enough to called depressive episode and last for two years or more.
- Major depression is c/by nihilistic delusions, negative thoughts, early morning awakening (disturbed sleep cycle)

- A 3 year old child has normal milestones except delayed speech. He likes to play on his own, has difficulty in concentration, making friends and relating to other people. What could be the diagnosis.
- A. Attention Deficit Disorder.

- B. Mental retardation.
 - C. Autism.
 - D. Specific Learning Disability.
- (Ans: Autism)

- A 9 year child disturbs other people, is destructive, interferes when two people are talking, does not follow instructions and cannot wait for his turn while playing a game. He is likely to be suffering from:
- A. Emotional disorders.
 - B. Behavioural problems.
 - C. No disorder.
 - D. Attention deficit hyperactivity disorder
- (Ans: D. Attention deficit hyperactivity disorder)

- A Middle aged person reported to psychiatric OPD with the complaints of fear of leaving home, fear of traveling alone and fear of being in a crowd. He develops marked anxiety with palpitations and sweating if he is in these situations. He often avoid public transport to go his place work. The most likely diagnosis is:

[AIIMS May'06]

- A. Generalized anxiety disorder.
- B. Schizophrenia.
- C. Personality disorder.
- D. Agoraphobia.

(Ans. D. Agoraphobia)

The person in the question has fear of surroundings or of being in exterior

Agoraphobia is commonest type of phobia. This is an example of irrational fear of situations. It is characterized by an irrational fear of being in places, particularly crowded places.

- A patient with Acute Psychosis, who is on haloperidol 20 mg/day for last 2 days, has an episode characterized by tongue protrusion, oculogyric crisis, stiffness and abnormal posture of limbs and trunk without loss of consciousness for last 20 minutes before presenting to casualty. This improved within a few minutes after administration of diphenhydramine HCl. The most likely diagnosis is:

[AIIMS May'06]

- A. Acute Dystonia.
 - B. Akathisia.
 - C. Tardive Dyskinesia.
 - D. Neuroleptic Malignant Syndrome.
- (Ans.A. Acute Dystonia.)

Explained in next qn.

- A schizophrenic patient, who is on haloperidol presents with torticollis and orofaciolingual movements. Most likely diagnosis is : [AIPGMEE' 2011]

- A. Acute Dystonia.
- B. Akathisia.
- C. Tardive Dyskinesia.
- D. Parkinsonism

(Ans.A. Acute Dystonia.)

Acute dystonias usually occurs early in the course of anti-psychotic medication.

Frequently present as torticollis, oculogyric crisis, swallowing and chewing difficulties (orofaciolingual movements) and masseter spasms. It is usually associated with high potency antipsychotics like, haloperidol, resperidone etc.

- A 30 year old man who was recently started on haloperidol 30 mg/day developed hyperpyrexia, muscle rigidity, akinesia, mutism, sweating, tachycardia and increased blood pressure. The investigations showed increased WBC count, increased Creatinine Phosphokinase. There is no history of any other drug intake or any signs of infection. The most likely diagnosis is: [AIIMS May'06]

- A. Drug overdose
- B. Neuroleptic Malignant Syndrome.
- C. Drug induced Parkinsonism.
- D. Tardive Dyskinesia.

(Ans.B. Neuroleptic Malignant Syndrome)

Neuroleptic Malignant Syndrome

It occurs with high dose of potent antipsychotics. Patient develops marked rigidity, hyperpyrexia, sweating, tachycardia and increased blood pressure. The offending drug should be stopped immediately.

- A 21 year old girl was brought to the psychiatric emergency after she slashed her wrists in an attempt to commit suicide. On enquiry her father revealed that she made several such attempts in the past mostly in response to trivial matters. She had marked fluctuations in her mood with tumultuous interpersonal relationships. Most probable diagnosis in this case is. [MP '08]

- A. Emotionally unstable personality disorder
- B. Generalized anxiety disorder
- C. Anti-social personality disorder
- D. Adjustment disorder

(Ans. A. Emotionally unstable personality disorder)

It is also k/as borderline personality disorder.

- ❑ A 25 year old man remains mute, holds saliva in mouth, has rigidity all over and maintains odd postures for prolonged periods of time. The most probable diagnosis is.[MP '08]

A. Dementia
B. Catatonia
C. Bipolar affective disorder
D. Factitious disorder

(Ans: Catatonia)

This is the typical presentation of patient suffering from catatonic type of schizophrenia. Bipolar affective disorders are c/by two extremes of mood-- mania & depression

- ❑ 12 year old female complains of headache, pain in the legs, recurrent vomiting. All physical and laboratory tests are normal. What is her most probable condition?

[AIIMS Nov'09]

A. Somatization
B. Conversion
C. Somatoform pain disorder
D. Generalized Anxiety Disorder

(Ans. A. Somatization)

- ❑ A 30 year old female complains of sudden onset of breathlessness, anxiety, palpitation and feeling of impending doom. Physical examination is normal. What is her most probable condition?

[AIPGMEE' 2011]

A. Panic attack
B. Conversion reaction
C. Acute psychosis
D. Anxiety Disorder

(Ans.: A. Panic attack)

The attack often begins with extreme fear and a sense of impending doom. The symptoms rapidly increase over a period of 10 minutes. There may be palpitations, tachycardia, dyspnea and sweating.

- ❑ A 3 year old girl with normal milestones, delayed speech, playing alone not able to make friends

[AIIMS May'10]

A. Autism
B. Attention deficit
C. Speech learning disorder
D. Mental retardation

(Ans. Autism)

In autism developmental milestones are normal but there is

impairment in social and peer group interactions. Delayed communication skills (delayed speech) is also noted.

- ❑ A child presents with unknown ingestion of substance with symptoms of mydriasis, delirium, tachycardia hot and dry skin, dry mouth. Probable cause

[AIIMS May'10]

A. Anticholinergic syndrome
B. Sympathomimetics
C. Cholinergic
D. Opioids
(Ans. Anticholinergic syndrome)

- ❑ A boy presents with symptoms of diarrhoea, rhinorrhoea, sweating, and lacrimation. Probable cause

[AIIMS Nov'10]

A. Cocaine withdrawal
B. Heroin withdrawal
C. Alcohol withdrawal
D. LSD withdrawal
(Ans. B. Heroin withdrawal)

Symptoms are consistent with opioid withdrawal.

- ❑ A 42 year old man , who complains of delusion and feeling of wealthlessness often. He used to consult his spiritual guru whenever he felt so. The family members are not convinced with the way, he progressing. He starts feeling that living is worthless and tends to take others on anger unnecessarily. Best treatment for him at this level would be:

[AIPGMEE'10]

A. Antidepressant only
B. Antidepressant + Antipsychotics
C. Antidepressant + Sessions with his spiritual guru
D. Antipsychotics + Behaviour therapy
(Ans. B. Antidepressant + Antipsychotics)

Pt. is in psychotic depression . When a depressive patient develops psychotic symptoms (here delusions) best to give a combination of antidepressant + antipsychotics

- ❑ A 45 year old business executive lady lost her business 1 year back. Following which she remains lethargic. Her mood is depressed and there is loss of appetite and insomnia lasting for more than 1 year. Which of the following is true for this patient?

[AIPGMEE'11]

- A. Antidepressant should be prescribed depending upon the side effect profile
- B. SSRI's are the most effective antidepressant in this lady
- C. Combination of 2 antidepressants is recommended.
- D. Patient does not require any treatment as it is a normal reaction.

(Ans. A. Antidepressant should be prescribed depending upon the side effect profile)

Pt. is in chronic depression following a stressor. In major depressive disorder antidepressants should be given for at least 6 months.

- A 40 year old man illicit relationship with his wife, and he also suspects them that they are trying to kill him by arranging some person. He is reverent to his elder brother, but he does not believe when his brother explains that his belief is contrary to the truth. He also feels that people are conspiring against him. He is having these problems for the past 2 months. He keeps to himself at home not in the office. But he attended work takes a keen interest in the news. Which of the following condition best explains this patient's profile :

[AIPGMEE'10]

- A. Schizophrenia
- B. Persistent delusional disorder
- C. Paranoid personality disorder
- D. Acute psychosis

(Ans. B. Persistent delusional disorder)

Pt. is suffering from delusion of infidelity and persecution. Thus this is a delusional disorder. Apart from the impact of the delusion(s), or its ramifications, functioning is not markedly impaired, and behavior is not obviously odd or bizarre, thus this is a delusional disorder.

Acute psychosis is c/by onset of symptoms within 2 weeks.

Schizophrenia requires a period of 6 month.

- A 36 year old married woman comes with complaints of feeling worthlessness since 6 months and a dull through out the day. She is not able to concentrate on things, she is anxious about participating in her official proceedings and even for being part of a crowd. She has not made any suicidal attempts and she has no authentic stressors to explain her symptoms. She also complaints of somatic symptoms like pain in the body and burning sensations, occasional palpitations. Music does not help her in elevating her mood. Which of the following condition best

explains this patient's profile :

[AIPGMEE'10]

- A. Mild depression
- B. Bipolar disorder
- C. Generalised anxiety disorder
- D. Mixed anxiety depression

(Ans. D. Mixed anxiety depression)

Pt. is suffering from Mixed anxiety depression. Mixed anxiety depression is a diagnostic category defining patients who suffer from both anxiety and depressive symptoms of limited and equal intensity accompanied by some autonomic features.

- A 45 years old male was admitted for CABG in a hospital for 2 weeks. Procedure was uneventful. He was discharged at a later date, he is not able to recollect names, phone numbers and his own house address. He is not agitative, dull or anxious. Most likely diagnosis is :

[AIPGMEE'10]

- A. Post-operative psychosis
- B. Post operative depression
- C. Post operative cognitive dysfunction
- D. Conversion disorder

(Ans. C. Post operative cognitive dysfunction)

Pt. is suffering from POCD (Post operative cognitive dysfunction). POCD is decline in cognitive function which persists for weeks to months after major surgery. Seen in elderly after major cardiac surgery. It is c/by impairment of memory, lack of concentration, impaired language comprehension, and social integration. Intraoperative factors e.g. hypotension, hypoxia, anesthesia, anaesthetic agent used, inflammatory response to CABG are thought to be responsible for such changes.

Post operatively this patient is neither dull nor anxious/agitative, so no sign of psychosis/ neurosis.

- A 20 year old boy complains of hearing of various voices, aggressive behaviour since 2 days. When asked to his family, they says that he has been muttering to self and gesticulating. There is no h/o psychiatric illness. Most likely diagnosis is :

[AIIMS Nov'10]

- A. Acute psychosis
 - B. Delirium
 - C. Dementia
 - D. Delusional disorder
- (Ans. A. Acute psychosis)

- A 35 years old male is a chronic smoker. His family insists on quitting smoking. He is thinking about quitting, but is reluctant to do so because he is worried that on quitting he will become irritable. This phenomena is :

[AIPGMEE'11]

- A. Precontemplation and preparation
 - B. Contemplation and extent of sickness susceptibility
 - C. Contemplation and cost factors
 - D. Precontemplation and cost factors
- (Ans. B. Contemplation and extent of sickness susceptibility)

There are 5 stages of behaviour change model.

1. Precontemplation - Not seriously considering change
2. Contemplation - Thinking about change
3. Preparation - Getting ready to make change
4. Action - Making behaviour change
5. Maintenance - Sustaining behaviour change until integrated into lifestyle.

- A young man 20 year old residing in metropolitan city in India is suffering from drug abuse. His perception of sensory modalities crosses over. For example he can feel the sounds and hear the colours. Most likely substance of abuse is :

[AIPGMEE'12]

- | | |
|--------------|--------|
| A. Cocaine | B. LSD |
| C. Marijuana | D. PCP |
- (Ans. B. LSD)

The main psychologic experience during LSD intoxication involves alterations of perception (sound, color intensity, crossover of sensory modalities) . Perception of sensory modalities crosses over, k/as synesthesia.

NOTES

GENERAL ONCOLOGY

Cancer Epidemiology

Common cancers in specific geographical areas

- South East, China --- Nasopharyngeal Ca
- Japan --- Adeno Ca of stomach
- South East Asia --- HCC
- Africa --- Burkitt's lymphoma

Cancer epidemiology: magnitude of problem worldwide

- M/c cancer in males worldwide: **Prostate Ca** [Incidence: prostate (33%) > lung (13%) > colorectal (11%)]
- M/c cancer in females worldwide: **Breast Ca** [Incidence: breast (32%) > lung (12%) > colorectal (11%)]
- M/c cause of cancer deaths in males: **Ca lung** [Lung > prostate > colorectal]
- M/c cause of cancer deaths in females: **Ca lung** [Lung > breast > colorectal]
- M/c cancer site (& also death) in both males / females: **Ca lung**

In India (According to Park's)

- M/c cancer in males – cancer of upper aerodigestive tract (oral cancer)
- M/c cancer in females – **Ca-cervix** > Ca breast

- Overall most significant risk factor for cancer is age
- M/c cancer that is increasing at the fastest rate worldwide is – malignant melanoma
- M/c cause of death in cancer patient ---infections leading to heart failure
- Major determinant of t/t outcome in cancer patient: tumour burden > physiological reserve (assessed by Karnofsky performance status)

Childhood Tumours

- M/c pediatric malignancy overall: **Leukemia** > lymphoma
Leukemias account for 1/3rd of all neoplasm in children. ALL is the commonest type (75%)
- M/c neoplasm in children <2 yr: Neuroblastoma
It is the second most common solid tumour in children second only to glioma/medulloblastoma

- M/c solid tumour in children---Brain tumours
- M/c renal neoplasm in children---Wilm's tumour
- M/c soft tissue tumour in children---Rhabdomyosarcoma

Metaplasia

- Metaplasia is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.
- The m/c epithelial metaplasia is --- columnar to squamous, as occurs in the respiratory tract d/ to chronic irritation (in chronic smokers normal columnar ciliated epithelium @ changes to stratified squamous epithelium)
 - Squamous to columnar metaplasia is seen in Barrett's esophagitis.
 - In vitamin A deficiency squamous metaplasia is seen in respiratory epithelium.
 - Dysplasia is the forerunner of carcinoma in situ.
 - Anaplasia refers to lack of differentiation and is the hallmark of malignant transformation.
 - Intestinal metaplasia is the most significant risk factor for development of gastric cancer.
 - Intestinal metaplasia is seen in Barret's esophagus.
 - Abnormal migration of totipotent cells results in → malignant teratoma

Staging and Grading of Tumours

Staging

- Is based on the size of primary tumour, nodal spread and blood spread." It is called TNM staging
- Staging establishes extent of disease and prognostic and therapeutic significance in most cancers
- Important cancer staging systems
 - Gleason's grading system --- for prostate cancer
 - Duke's system --- for colorectal cancer

Grading

- Is based on is nuclear pleomorphism, cellularity, necrosis, cellular invasion and no. of mitoses. (depending upon the type of tumour)
- Grading is histological determination and refers to the degree of cellular differentiation
- Important cancer staging systems
 - Gleason's grading system --- for prostate cancer
 - Duke's system --- for colorectal cancer

- ↑ing grades denotes increasing degree of anaplasia.
- ↑se in laminin & fibronectin receptors show invasiveness of tumour.
- Usually grade has less prognostic value in most cancers (but exceptions are soft tissue sarcoma, astrocytoma, transitional cell carcinoma, HD & NHL in which tumour grade has great clinical significance)

PROGNOSTIC FACTORS IN CANCERS

Cancer	Most important prognostic factor
• Soft tissue sarcoma	Grade
• Malignant mesenchymal tumour	Grade
• Breast Carcinoma	LN-involvement (esp axillary nodes)
• Male breast Ca	LN-involvement
• Stomach cancer	Depth of invasion >LN
• Carcinoid tumours, Pancreatic endocrine tumours	Presence of liver metastasis
• Colorectal	Depth of invasion, LN status
• Hepatoblastoma (HCC)	Resectability of primary tumour, extent at diagnosis
• Wilm's	Histology >stage
• RCC	Stage (Robinson's)
• Ca bladder	Depth of invasion
• Endometrial cancer	LN involvement
• Penile cancer	Presence & extent of superficial inguinal LN involvement (Nodal status)
• Hodgkin's lymphoma	Staging
• Langerhans cell histiocytosis	Age & degree of organ involvement
• AML	Age at diagnosis
• Malignant melanoma	Stage (tumour thickness)

- In colon cancer single m/c Px factor → stage of d/s.
- In colon cancer m/c independent Px factor → LN status.

- Indicators used to assess nutritional status and intervention threshold in cancer patient are
 1. >10% unexplained weight loss
 2. S. transferrin level <1500 mg/L
 3. S. albumin <3.4 g/dl

Curable malignancies

- Childhood cancers---ALL,NHL,Wilm's, Ewing's, Rhabdomyosarcoma, RB
- Adult--- Acute leukemias, Ovarian ca,
- Other--- Chorio ca, Testicular ca, Hodgkin's

Screening

- Screening has been useful in bringing down mortality in --- Ca cervix, Ca Breast, Ca Colon
- Important screening methods :

Cancer	Screening Method
1. Breast cancer	Triple test
2. Ca cervix	Pap smear
3. Ca colon	sigmoidoscopy
4. Ca cervix	Pap smear

- Tissue resistant to tumour invasion
 - Mature cartilage
 - Elastic tissue artery
- All cancers metastasize except
 - Glioma of CNS
 - BCC of skin
- Common cancers that invade blood vessels
 - Renal cell carcinoma (RCC)
 - Follicular Ca of thyroid
 - HCC
- Retrograde metastasis is seen in
 - Krukenberg's tumour
 - Metastasis of Ca prostate to supraclavicular LN
 - Metastatic deposit in adrenals from Ca lung
 - Metastatic deposit in ovaries from g.i. tumours.

Tumours showing CSF spread

- Ependymoma
- Oligodendroglioma
- Anaplastic astrocytoma
- Glioblastoma multiforme

Sarcoma that spread via lymphatics

Prophylactic LN removal is done in these paradoxical tumour which metastasize via lymphatics:

- Synovial cell sarcoma
- Clear cell sarcoma
- Angiosarcoma
- Rhabdomyosarcoma
- Epithelial sarcoma

- o Malignant fibrous histiocytoma
[Mnemonic : Scare Me]
- *Ames assay / test is useful in screening for potential carcinogens, detects mutagenicity. This assay uses strain of salmonella typhimurium*
- *Test used for mutagenicity of chemicals ----- Ames test.*
- *Skip metastasis is seen in bronchogenic carcinoma*

BIOPSY FOR NEOPLASMS

Incisional biopsy

- o Sample is taken from edge of the lesion as in ulcer, not from centre (exceptions – *biopsy is taken from the centre of the lesion in post-radiation ulcer and syphilitic gumma*)
- o Preferred for large, usually >5 cm deep soft tissue mass.
- o **C/ind in case of melanoma** (here excisional biopsy is preferred)
- o In secondaries in LN, FNAC is preferred. If it fails to give information, incisional biopsy is done

Excisional biopsy

- o Surgical removal of an entire gross lesion. E.g. LN biopsy in case of lymphoma
- o Recommended for <5 cm lesion or in conditions when gross lesion has to be removed e.g. lymphoma, **melanoma**

FNAC

- o Rapid and minimally invasive technique for the biopsy of palpable superficial tumour
- o Useful in parotid, thyroid, enlarged LN, breast and all other surface lesions
- o In LN it is useful for detecting secondaries and TB
- o In follicular carcinoma of thyroid it is not useful
- o **It is absolutely C/ind in testicular tumour**
- o *Frozen section biopsy* is done in carcinoma breast or in follicular carcinoma of thyroid when FNAC fails
- o *Core needle biopsy* cuts slices of tissue. Histologic information obtained is more than FNAC. Frequently used for prostate, breast, and liver masses.

Sentinel Lymph Node biopsy is done in

- o Ca Cervix (Pelvic & paraaortic LN)
- o Ca vulva, Ca endometrium
- o Ca breast (in clinically node -ve d/s)
- o Melanoma
- o Carcinoma penis

Exfoliative cytology is useful in

- o Ca cervix
- o Ca bronchus/ lung
- o Ca stomach
- o Transitional cell carcinoma bladder

TUMOUR MARKERS

β-HCG

- o Placental hormone used for monitoring of gestational trophoblastic tumours
- o ↑ed mainly in **non-seminomatous GCTs** of testis/ovary.
- o Frequency of elevation in
 1. Seminoma 15%
 2. Teratoma 42%
 3. Embryonal carcinoma 50%
 4. Choriocarcinoma 100%
- o Never ↑ed in yolk sac tumour.

	Marker	Raised in
Hormonal	β-HCG	Trophoblastic tumour (chorioma/NSGCT)
	Calcitonin	Medullary Ca thyroid
	VMA & catecholamines	Pheochromocytoma
Isoenzymes	PAP (prostatic acid phosphatase)	Ca- prostate
	PLAP (Placental alk. phosphatase)	Dysgerminoma, testis, trophoblastic tumors
	NSE	SCLC (Oat cell/small cell lung Ca), Neuroblastoma
	LDH	Lymphoma (LDH ₁), Ewing's sarcoma
Oncofetal antigens	AFP	Liver Ca, NSGCT, Endodermal sinus tumour (Yolk sac tumour)
	CEA	Mainly in adenocarcinoma colon/Colorectal cancer Also in adeno carcinoma of pancreas/lung (SCLC)/ stomach/ breast/ ovary
Mucins	CA-15.3	Ca breast
	CA-19.9	Ca pancreas, colon
	CA-125	Ca ovary

{Remember from above downwards breast/pancreas/colon/ovary : 15.3/19.9/125}

- Oncofetal antigens are normally expressed in embryonic tissue (embryonic antigens) but not in adults eg. :- CEA, AFP
- Differentiation antigens are peculiar to differentiation state at which cancer cells are arrested. eg :- CD-10 (CALLA antigen), PSA
- AFP is a specific marker of hepatoblastoma.
- PSA is the most sensitive marker for prostatic Ca
- Bence Jones's protein is tumour marker for MM
- Tumour markers for SCLC ---CEA, NSE, bombesin
- CEA is also increased in hepatitis, IBD (UC/CD), pancreatitis
- CA-125 positivity in stage I ovarian cancer is ~40%

ONCOGENESIS

CHEMICAL CARCINOGENES & CANCERS

Initiators

- Polycyclic hydrocarbons --- SqCC of lung, oropharynx, cervix, larynx
Transitional cell ca. of bladder, pancreatic adenocarcinoma
- Arsenic --- Basal CC & epidermal hyperplasia, Ca lung
- Benzene --- Leukemia (AML)
- Chromium, Radon, Uranium --- Lung Ca.
- β -naphthylamine, aniline dyes --- Urinary bladder Ca.
- Nitrosamines --- Esophageal ca., gastric Ca.
- Azodyes, aflatoxins, OCPs, thorotrast, alcohol --- Hepatoma (HCC)
- Vinyl chloride, Arsenic, Thorotrast --- Angiosarcoma of liver
- Immunosuppressants --- NHL
- Alkylating agent --- AML, bladder ca

Promotors

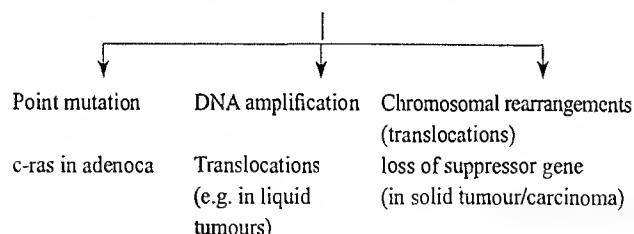
- Saccharin -- Bladder Ca.
- Estrogens -- Ca breast, Endometrial Ca, Liver Ca etc.
- DES(prenatal) -- Clear cell vaginal adenocarcinoma
- Phenacetin -- Transitional cell Ca of renal pelvis and bladder

- Ethmoidal sinus adenocarcinoma is seen in wood workers, while SqCC is seen in workers of nickel industry.

Mechanisms that lead to cancer are

- Either inactivation of tumour suppressor gene or
- Activation of oncogenes

1. Activation of oncogenes : 3 mechanisms



- Point mutations of c-ras oncogene is seen in adenocarcinomas.
- Gene amplification of c-erb B2 is seen in breast cancer

Translocations

Oncogenes	Translocations	Examples
abl, bcr	t (9:22)	CML, AML, ALL type 3
c-myc	t (8:14)	Burkitt's lymphoma, ALL FAB Type3, Immunoblastic B-cell lymphomas
	t (2:8) (p11, q24)	Burkitt's lymphoma, B-ALL
	t (3:8)	RCC
	t (6:14)	Cystadeno Ca of ovary
P53, erb	15:17	M ₃ AML (Acute promyelocytic)
Ets-1, sis, fl-1	11:12	Ewing's
	t (x:18)	Synovial cell sarcoma
Bcl-1, bcl-2	14:18	B-cell follicular lymphoma
	8:21	AML with maturation M2

- BCL-2** is apoptosis inhibitor gene. It protects lymphocytes from apoptosis.
- TP-53** or P53 promotes **apoptosis** and cell death. It is a suppressor gene, inactivation of p53 by point mutation may lead to colorectal, breast, lung & CNS cancers
- Bax and IgF-BP3** are k/as cell death genes.
- RAS** : M/c organic mutation in human cancers. c-erb B1 Oncogene RAS activation by point mutation can lead to cancers of lung, colon, pancreas, ovary and leukemias.
- There are 2 main mechanisms of inactivⁿ of suppressor genes
 - Point mutation
 - Deletion → leading to loss of functional product and loss of heterozygosity in tumour DNA.

TUMOURS A/W SUPPRESSOR GENE INACTIVATION

Subcellular location	Tumour suppressor gene	Remark	Function	Tumour a/w somatic mutation	Chromosomal location of gene	Tumour a/w inherited mutation
1. Cell surface	TGF- β Receptor		Growth inhibition	Ca Colon		Unknown
	ϵ cadherin		Cell adhesion	Ca stomach		Familial Gastric Ca
2. Cell membrane	PTCH (Patched)	Receptor for Hedgehog protein	Regulates TGF- β & PDGF RA & RB	Sporadic BCC		Gorlin syndrome /nevroid basal cell carcinoma syndrome, esophageal SqCC, trichoepitheliomas, transitional cell carcinomas of the bladder, holoprosencephaly
2. Inner plasma membrane	NF-1		Inhibition RAS signal transduction & p21 cell cycle	Neuroblastoma	17	NF-1, Sarcoma.
3. Cytoskeletal	NF-2		Cytoskeletal stability	Schwannoma & meningioma	22	NF-2, Acoustic schwannoma, Meningioma
4. Cytoplasm/ cytosol	APC/ β catenin		Inhibition of signal transduction	Ca stomach, colon, pancreas, liver, Melanoma		FAP, Colon cancer Gardner syndrome
	PTEN		PI-3 kinase signal transduction	Ca endometrium, prostate		Cowden syndrome (Epithelial cancers)
	SMAD 2&4		TGF- β signal transduction	Ca Colon, pancreas		-
5. Nucleus	Rb		Cell cycle regulation	Sporadic Retinoblastoma & osteosarcoma, Ca breast, colon, lung	13	Familial retinoblastoma, osteosarcoma
	P53	Guardian of genome	Cell cycle arrest & apoptosis in response to DNA damage	Most human cancers	17p13.1	Li- Fraumeni syndrome, Multiple carcinomas & sarcomas
	WT-1		Nuclear transcription	Wilm's	11p	Wilm's
	p16 (INK 4a)/ CDKN2A		Inhibition of cyclin dependent kinase \rightarrow Cell cycle regulation	Pancreatic, breast, esophageal cancers		Malignant melanoma
	BRCA-1		DNA repair	-	17	Ca female breast & ovary (sometimes colon, prostate)
	BRCA-2		DNA repair	-	13	Ca male & female breast
	KLF-C		Transcription factor	Prostate		-

PROTO-ONCOGENES & THEIR EXPRESSION IN NEOPLASMS

Category	Proto-oncogene	Mode of activation	Cancer of
β PBGF	c-cis	Overexpression	Astrocytoma, osteosarcoma
FGF	hst1	Overexpression	Stomach
FGF3	INT 2	Amplifica ⁿ	Bladder, breast, melanoma
EGF-R	c-erb B1	Overexpression	SqCC of lung, glioma
Tyrosine kinase3	c-erb B 2 (HER2-ncu)	Amplifica ⁿ	Sporadic Breast Ca
Stem cell factor-R	RET	Point mutation	Leukemia, MEN2A/B, Familial MTC (thyroid)
Abnormal membrane	KIT	Point mutation	GIST, Seminomas, leukemias
	c-abl	Translocation	CML, ALL
GTP binding proteins	k RAS	Point mutation	Colon, lung, pancreas
	hRAS	Point mutation	Bladder, kidney
	n RAS	Point mutation	Melanoma, hematological cancers
Nuclear regulatory proteins	c-myc	Amplifica ⁿ	Burkitt's
	N-myc	Amplifica ⁿ	Neuroblastoma
	L-myc	Amplifica ⁿ	SCLC lung

DIETARY FACTORS a/w \uparrow RISK OF CANCERS

Diet factor	\uparrow risk of
Beer consumption	Rectal Ca
Smoked fish	Stomach Ca
High dietary fibres	Intestine
Beef consumption	Bowel
High fat	Breast, colorectal

Protective Role

- Tomato sauce lycopene is a/w \downarrow risk of prostate cancer.
- Garlic is a/w \downarrow risk of bladder cancer.
- Juice of cranberry protects against UTI, cystitis & bladder cancer.

- Pomegranate & cranberry juice have role in protection against prostate & bladder cancer.

Primary prevention modalities in cancer

- Aspirin ---- \downarrow risk of esophageal, stomach, colon, rectal cancer
- Isotretinoin (vit E, Se) ---- \downarrow leukoplakia in the lungs and GIT
- Tamoxifen ---- \downarrow risk of 2nd primary malignancy in spared breast
 \downarrow incidence of breast cancer in women who have a strong F/H of breast carcinoma
- Calcium ---- \downarrow risk of colon Ca

MICRO-ORGANISMS & CANCERS

Agent	Lymphoid malignancies	Other malignancies
EBV	Burkitt's, Hodgkin's, Primary CNS large B-cell Lymphoma	Nasopharyngeal ca
HTLV-1	Adult T-cell Leukemia / Lymphoma	Tropical spastic paraparesis
HTLV-2	HCL (Hairy cell leukemia), Chronic T-cell lymphoproliferative disorder	
HTLV-3		AIDS
HPV-1,4	Skin & plantar warts (Benign Sq papilloma)	
HPV-2,7	Butcher's warts	
HPV-6,11	Condyloma acuminata	
HPV-16, 31	CIN, SqCC cervix, anal canal, penis	
HPV-18	Adenoca Cervix	
HHV-8	Kaposi's sarcoma,	Primary effusion lymphoma
HIV	Diffuse large B cell (immunoblastic), Burkitt's lymphoma	
HCV	Lymphoplasmacytic lymphoma	
H. Pylori	MALT Lymphoma	
Boca virus	Ca urinary bladder	

→ *HSV-1 is NOT a/w malignancy*

SMOKING is related to

- GIT cancers
 - Ca - Kidney
 - Ca - Pancreas
 - Ca - Urinary bladder
- *Tobacco abuse causes cancer of buccal mucosa > tongue*
 → *Smoking is protective against Ca endometrium*

OBESITY predisposes to the cancers of

- Kidney
- Breast
- Endometrial
- Ca - Prostate
- Colorectal, GB

Hormone dependent tumours

- Papillary Ca of thyroid ---- TSH dependent
- Breast CA ---- Progesterone dependent
- Endometrial Ca ---- Estrogen dependent
- Prostate Ca ---- Androgen dependent

Hypercalcemia is seen in

- Bronchogenic Ca
- Renal cell Ca
- Breast Ca
- Plasma cell myeloma (Multiple myeloma)

ONCO-PATHOLOGY

Nuclear abnormalities present in malignant cells :

- ↑ Nuclear to cytoplasmic ratio, hyperchromatic nuclei
- ↑ ed S-phase (↑ ed synthesis of DNA is a/w aggressiveness)
- Irregular nuclear borders, large irregular nucleoli (↑ synthesis of RNA)
- Longer cell cycle than the parent tissue

Metabolic features of malignant cells:

- Anaerobic glycolysis
- Degradative enzymes
- Lack of cohesiveness

- Lack of contact inhibition in culture
- Transplantability into susceptible animals.

- *Adhesion molecule CD-44 is important in vascular dissemination of tumour cells.*
- *Laminin receptors assist in their movement through tissue (cell to cell adhesion, cell-BM adhesion, cell-ECM adhesion).*
- *Bostamistat, fumagillin & angiostatin (TNP-470) have anti-metastatic role. Avastin inhibits primarily angiogenesis.*
- *M/c initial site in a lymph node of carcinomatous spread ---- Subcapsular sinus*
- *EM finding in vascular tumor ---- Weibel-Palade bodies*
- *Chemical factor a/w cachexia in cancer pt ----- TNF-α secreted by host macrophages & cancer cells.*
- *Growth factors involved in the invasion of tissue by malignant cells ----- TGFα & β + FGF.*

Immunohistochemical stains

- S-100 antigen ---- for tumours of neural crest origin e.g. neuroendocrine tumours, APUD tumours, melanoma, SCLC, carcinoid tumours, neuroblastoma, astrocytoma
- CD1 antigen ---- Tumours of histiocytic origin
- HMB-45 ---- Most specific for malignant melanoma
- CD45 ---- Malignant lymphoma, for leucocyte malignancy
- Desmin ---- Specific for muscle derived sarcomas
- Cytokeratin** ---- Carcinomas, epithelial cancers
- Myoglobin ---- Rhabdomyosarcoma
- Factor VIII ---- Kaposi sarcoma, vascular tumours/ angiosarcoma
- Thyroglobulin ---- Thyroid cancer (except medullary Ca)

- *Markers for neural/ NET (neuroendocrine tumours) are ---NF, NSE synaptophysin, Chromogranin*
- *For glial tumours ---GFAP*

TUMOURS: COMMON POINTS

Pulsating tumours

- Telangiectatic Osteogenic sarcoma
- Angioendothelioma (Hemangioendothelioma)/ Angiosarcoma of bone
- Aneurysmal bone cyst
- Rarely GCT

- *Pulsating vascular skeletal metastasis*
Secondaries from RCC (renal tumour) & from Follicular Ca thyroid

Lytic expansile lesion

- Ca thyroid
- RCC (telangiectatic variant)
- Melanoma
- Pheochromocytoma

- ➔ *Pulsating vascular skeletal metastasis are seen in --- Follicular carcinoma thyroid*
- ➔ *In osteoclastoma characteristic "egg shell crackling" is felt on palpation but it is a non-pulsatile tumour.*

Small "blue round cell" tumour of childhood

Histology of these tumours reveal sheets of uniform small round, blue cells

- Neuroblastoma, Wilm's at times
- Malignant lymphoma
- Rhabdomyosarcoma
- Ewing's sarcoma
- Retinoblastoma

PNET (Primitive Neuro Ectodermal Tumours)

They arise from primitive (undifferentiated) nerve cells.

- In CNS: Medulloblastoma, pinealoblastoma, supratentorial cerebral tumours
- Peripheral : Soft tissue Ewing's sarcoma

NET (Neuro Endocrinal Tumours)

- They arise from primitive (undifferentiated) nerve cells.
- 69% of NET are located in the GI tract (stomach, pancreas, intestines) and are collectively called gastroenteropancreatic neuroendocrine tumors (GEP-NET). GEP-NET include carcinoid tumors and pancreatic NET.
- 60% of diagnosed NET are functioning. They may secrete peptides which cause symptoms.

GIST

- Gastrointestinal stromal tumours.
- Arise from intestinal cells of Cajal.
- M/c site stomach (45-60%), small bowel (30%), esophagus & rectum (10%).

- Metastasis to liver, omentum, peritoneum. Lymphadenopathy is unusual.
- C-kit proto-oncogenes are involved, which act thru tyrosine kinase. Overexpression of CD117.
- Dx: PET scan is gold standard for Dx of GIST.
- Rx: Excision → if recurrence → Sunitinib/ imatinib.

PRE-MALIGNANT CONDITIONS of cancers

- BCC of skin --- Arsenic/ tar keratoses
- SqCC of skin --- Actinic Keratosis, cutaneous horn
- SqCC of oral cavity --- Erythroplakia (more aggressive), leukoplakia, submucous fibrosis, melanosis
- SqCC of Penis --- Bowen's disease, erythroplakia of Queyrat, papilloma
- GB cancer --- Porcelain GB, Choledochal cyst, Gall stones
- Gastric adeno carcinoma --- Chronic atrophic gastritis (seen in pernicious anemia, H. pylori infection)
- Colon/ colorectal cancer --- UC, Pigment cirrhosis, Villous adenoma, familial polyposis
- Gastric adeno carcinoma --- Chronic atrophic gastritis (seen in pernicious anemia, H. pylori infection)
- Breast cancer --- Atypical ductal hyperplasia
- Medullary ca. of thyroid --- C-cell hyperplasia

Other Premalignant conditions

- Hamartomas
Neurofibromatosis, VHL syndrome, Tuberous sclerosis, multiple exostoses, Peutz Jeghers
- Genodermatosis
Xeroderma pigmentosa, Albinism, Polydysplastic epidermolysis bullosa
- Immuno deficiency d/s
Wiskott Aldrich, X-linked -agammaglobulinemia

- ➔ *Inherited predisposition to CNS tumours is seen in --- NF, VHL syndrome.*
- ➔ *Dowling Degos d/s is an AD genodermatosis.*

Inherited predisposition to cancer

- *Inherited predisposition to cancers is seen in some familial cancers with AD inheritance and in some syndromes*
 - Familial retinoblastoma
 - FAP or FPC (Familial adenomatous polyposis of colon)
 - NF1 and NF2
 - VHL syndrome
 - MEN
- *Familial cancers are*
 - Cancers which run in family (first degree relatives)
 - Breast cancer
 - Ovarian cancer
 - Uterine cancer
 - Some colonic cancers
- *Syndromes a/w defective DNA repair (AR inheritance)*
 - Xeroderma pigmentosum, Ataxia-telangiectasia, Bloom syndrome, Fanconi anemia
- *Inherited disorders a/w ↑ed chromosomal fragility*
 1. Ataxia-telangiectasia
 2. Bloom syndrome
 3. Fanconi anemia
 4. Kostman syndrome

Mixed tumours

- Pleomorphic adenoma of parotid
- Wilms' tumour
- Breast Carcinoma (Fibroadenoma & Cystosarcoma phyllodes)

RADIATION INDUCED TUMOURS/Cancers

- Acute leukemia (most common)
- Papillary Ca of thyroid
- Breast cancer
- Lung cancer (radon gas from uranium)
- Angiosarcoma of liver (thorotrast)
- Skin cancers eg. BCC, SqCC, Malignant melanoma (UV-B induced)
- Brain tumors.
- Osteosarcoma.
- Lymphangiosarcoma (Thorium induced).

CANCER RADIOTHERAPY

Radiation Sensitivity of Tumours

Sensitivity	Examples
1. Highly sensitive (RT is TOC)	- Lymphoid tumours (Lymphocytes are most sensitive) - Anaplastic tumours - Embryonal tumours
2. Moderate sensitive	- Reticulum cell sarcoma - Squamous cell carcinoma
3. Least sensitive	- Tumours of mesenchyme - Osteo/fibro-sarcoma - Adenocarcinoma

R_T is T/t of choice in

- Lymphomas
(HD & NHL early stage)
- Burkitt's lymphomas
- Seminoma,
- dysgerminoma
- Ewing's sarcoma
- Neuroblastoma
- Medulloblastoma

R_T is not useful in

- Adeno carcinoma,
Pleomorphic adenoma
(Salivary gland neoplasm)
- Non - seminoma,
- Osteosarcoma
- Malignant melanoma
- Carotid body tumour
- Pancreatic carcinoma

R_T has only palliative role in

- Prostate & breast Ca when bone metastasis is +nt.
- Advanced stage lung & esophagopharyngeal Ca.
- Gastric cancer & sarcomas in brain metastasis.
- Multiple myeloma

Intra-operative R_T is used in

- Head and neck cancers
- Gastric carcinomas
- Pancreatic carcinoma
- Under trial in colon Ca.
- Soft tissue sarcoma in retroperitoneum

IMP. FORM OF RADIATION

- *Emergency radiotherapy* is given in pancoast tumour.
- *Inverted Y-field radiation* (Mantle field radiation to pelvic / para-aortic LN) is given Hodgkin's lymphoma (early stages, stage I & II)
- *Whole body radiation* (Total skin electron irradiation) is given in mycosis fungoides (Sezary syndrome), CML, BMT recipients, advanced low grade NHL, ca endometrium stage III & IV.

CANCER CHEMO

Adjuvant Chemotherapy

- T/t of minimal residual disease after surgery or radiotherapy (Micrometastasis T/t)
- Used for : ALL, Fibrosarcoma

Combination Chemo (CHEMORADIATION)

- Used for :
 - Carcinoma anal canal
 - Pediatric tumors: Wilm's, Ewing's, Rhabdomyosarcoma
 - Hodgkin's d/s (Stage II & III)
 - Limited small cell lung Ca (sclc)
 - Inflammatory breast Ca
- Also favorable response in :
 - NHL, head/neck Ca,
 - Esophagus Ca,
 - Colorectal cancer, sarcoma.

Neo-adjuvant Chemotherapy

- Administration of drugs before curative surgery/RT
- To destroy micrometastases & to reduce the size of the tumour
 - In head & neck cancers (cisplatin/5-FU)
 - Ca esophagus
 - Osteosarcoma
 - Some pediatric solid tumors
 - Ca breast
 - Lung non-small cell
 - Locally advanced Ca larynx (cisplatin/ 5-FU)

Regression of tumours

- *Spontaneous regression of tumours is seen in ---*
Neuroblastoma, malignant melanoma, some blastomas (e.g. retinoblastoma)
- *Regression in response to chemotherapy is seen in ---*
Choriocarcinoma, Burkitt's lymphoma
- *Removal of primary tumour leads to regression of metastases ---*
RCC
 - Remember: Spontaneous regression is not seen in osteosarcoma.
 - In some cases of lymphoma, splenectomy is a/w regression of disease at remote sites (abscopal effect).

ANTI-CANCER DRUGS

Chemotherapy Drug of Choice for

- CML ----- Imatinib, hydroxyurea
- Pancreatic cancer ----- Gemcitabine
- Esophageal cancer ----- Cisplatin

→ Arsenic is a therapeutic modality for t/t of APL (acute promyelocytic leukemia)

Chemotherapeutic drug induced toxicities and their prevention T/t

Drug	Toxic compound & toxicity	Prevention / T/t Remark
Cyclophosphamide	Acrolein → Hemorrhagic cystitis Chemical cystitis)	Bladder irrigation with 0.9% saline or NAC, Systemic mesna
Ifosfamide (Prodrug)	Chloroacetaldehyde → ATN, neurotoxicity Acrolein → Hemorrhagic cystitis	Neuro/nephrotoxicity is more than cyclophosphamide.
Mtx	BM toxicity, mucosal toxicity	Folinic acid (leucovorin) Alkalinization of urine is required
Busulfan	Skin pigmentation and Pulmonary fibrosis	Switch over to melphalan
Anthracyclines -Doxorubicin -Daunomycin -Idarubicin	Cardiotoxicity	MUGA scan to assess toxicity Dexrazoxane (Iron chelator), Mitoxantrone
Cisplatin.	Nephrotoxicity	Amifostine

→ Doxorubicin causes DCM (dilated cardiomyopathy) with loss of myofibrils & vacuolation. Muscle fibres become wavy & there is loss of spindle orientation.

→ Oprelvekin (recombinant IL-11) used in treating and preventing chemotherapy induced thrombocytopenia.

→ Tacrolimus is a/w dose limited nephrotoxicity

→ Leflunomide is a/w diarrhoea, rashes, hair loss, thrombocytopenia, raised transaminases.

- Aprepitant is a selective high affinity neurokinin-1 receptor antagonist that is effective in preventing chemo therapy induced nausea.
- Floxuridine is a newer drug for hepatic metastasis of colonic cancer. It may cause sclerosing cholangitis.

Anti- Cancer Drug Ad/e Comparison

Category	Drug	Heart	Lung	Liver	GU-Kidney	GI (A/E Mtx)	PNS/CNS	BM
Alkylators	Cyclophosphamide	+	+	-	++ (bladder)	+	-	+++
	Nitrosoureas : Carmustine	+	+	+	+	+	- (Used in brain tumour)	+++
	Nitrosoureas : Streptozocin	-	?	-	+++	+	-	+
	Cisplatin	-	?	-	+++	++	++/+	+
Intercalaters	Doxorubicin	+++	+	-	-	+	-	+++
	Dactinomycin	+	?	- (Replaces Mtx in chorioca if jaundice dvps)	-	++	-	-
Others	Mtx	-	+	+	++	-	0/+++	+++
	5-FU	+	-	+	-	+++	-/+	+++
	Bleomycin	-	+++ (Pulm. fibrosis)	-	-	+	-	+
	Vincristine	-	-	-	-	++	+++/+	-
	Vinblastine	-	-	-	-	++	+++/+	+
	Etoposide	?	?	-	-	+	+/-	+++
Conclusion		?	A/E 5-FU, cisplatin, vinca	-	-	A/E Mtx	+/-	A/E Vincristine, L-asparaginase

- Least antiemetic drug is methotrexate as there is no GI side effects.
- Bortezomib (Velcade)* is a **proteasome inhibitor** (reversible inhibitor of the chymotrypsin like activity of 26-S proteasome that degrades ubiquitinated proteins), effective in multiple myeloma.
- Bexarotene* activates retinoid X-receptor used in mycoses fungoides (CTCL).
- Revlimid* inhibits $TNF\alpha$, effective in multiple myeloma and MDS..

Oral small molecule tyrosine kinase inhibitors

- Imatinib mesylate (Gleevec)**
Used in CML
- Gefitinab (Iressa)**
EGFR tyrosine kinase inhibitor (Her1 or Erb-1) for advanced lung/ breast cancer
- Lapatinab (Iressa)**
Orally active drug which reversibly blocks phosphorylation of the EGFR, ErbB2, and the Erk-1 and-2 and AKT kinases; it also inhibits cyclin D protein levels in human tumor cell lines and xenografts.
- Efaproxiral* enhances the effectiveness of radiation therapy

in brain tumour.

- **Temozolamide** : Brain tumour.
- **Vinorelbine** a semisynthetic vinka alkaloid for SCLC.
- **Topotecan and Irinotecan** are semisynthetic analogue of camptothecin, they interact with DNA topoisomerase (used for metastatic ca of ovary, SCLC)
- **Fosfestral** is a phosphate derivative of stilbestrol. Used in prostate Ca.
- **Ftorafur** is a recently introduced 5-FU congener used orally.
- **Gemcitabine** is a pyrimidine antagonist, acts by inhibiting DNA synthesis, used in pancreatic carcinoma.
- **M/c** cause of dose limitation of chemotherapeutic drug is --- BM depression/ Myelosuppression.

OTHER MODES OF CANCER T/T

IMRT (Intensity Modulated Radio-Therapy)

- Prostate cancer.
- Head and neck
- CNS tumours
- Early breast cancers

Prophylactic surgeries to prevent development of cancer

- **Total colectomy** ---- to prevent colorectal cancer in patients with **familial polyposis** and **UC** (as they have 100% malignant transformation rate)
- **Prophylactic total thyroidectomy** ---- Done in childhood in patients of **MEN-2** with **RET** protooncogene mutations to prevent medullary Ca-thyroid
- **B/L mastectomy** ---- in patients with infiltrating (invasive) lobular carcinoma
- **Oophorectomy** ---- To prevent ovarian ovarian Ca risk in familial cancer syndrome
- **Orchiectomy** ---- In patient with undescended testis to prevent development of testicular Ca.

Vaccines effective in cancer prevention

- **Hepatitis B vaccine** ---- effective in preventing hepatitis & HCC d/to chronic HBV infection
- **HPV vaccine** ---- for cervical cancer
- **H. pylori vaccine** ---- for gastric cancer (under trial)

Non-specific immuno (Biologic) therapy

- **BCG**: intravesical BCG in patients with superficial bladder cancer
- **Levamisole**: Colorectal carcinoma
- **IFN- α** : melanoma, lymphoma
- **Cytokines**: Role in RCC, metastatic melanoma
- **Corynebacterium parvum** – ovarian carcinoma

→ *Levamisole, BCG and Corynebacterium are immuno stimulators*

→ *Adoptive immunotherapy is under trial with lymphokine activated killer (LAK), IL-2, etc.*

→ *Best method of stem cell harvesting for post high dose chemotherapy patient ---- Through a blood cell separator*

INTERFERONS in CANCERS

	Role in cancers	Other diseases
IFN α	Best result in HCL, CML Moderate effect in - Lymphoma - Epidemic kaposi sarcoma (AIDS related) - Multiple myeloma - Malignant melanoma (for adjuvant Rx)	
IFN β		Multiple sclerosis
IFN γ		CGD (Chronic granulomatous d/s)

Calcineurin inhibitors

- Tacrolimus
- Cyclosporine

Regional Therapy

- Delivery of drugs using arterial supply allows high level of drugs at site and systemic toxicity is lessened.
- Regional limb perfusion: In t/t of extremity melanoma and sarcomas, melphalan and TNF are used.
- Isolated hepatic artery infusion of floxuridine, which is completely extracted on its 1st pass metabolism through the liver, is used for t/t of unresectable liver metastases of colorectal cancer.

MONOCLONAL ANTIBODIES (Mabs)

Polyclonal or monoclonal antibodies are used to provide passive immunity.

Mab	Target (Ab against)	Useful in
1. Rituximab	A chimeric Ab against B-cell antigen CD-20	NH Lymphoma
2. Trastuzumab (Herceptin)	Recombinant humanized Mab against HER-2/ neu (C-erb B2) gene	HER-2/neu receptor+ metastatic breast ca.
3. Alemtuzumab	Humanized Mab against CD-52 antigen	Resistant CLL
4. Cetuximab	Chimeric human/animal recombinant mab	Metastatic colorectal cancer with EGRF++
5. Bevacizumab	Ist anti-angiogenic agent Vs. VEGF	Metastatic colorectal cancer

Radiolabeled and toxin-linked antibodies

	Labeled with	Useful for t/t of
Ibritumomab tiuxetan	Y-90 labeled Ab against CD-20	Low grade NHL
Tositumomab	Linked to ^{131}I	Low grade NHL
Denileukin difitox	Recombinant-DNA derived cytotoxic protein (ONTAK) (diphtheria toxin frag, IL-2)	Cutaneous T-cell lymphoma
Gemtuzumab Ozogamicin	Antibody to CD-33 linked to calicheamicin (potent anti tumour antibiotic)	Refractory AML

→ *Oprelvekin* --- Recombinant IL-11 used for prevention and t/t of thrombocytopenia induced by cancer chemotherapy

Hormonal therapy

- *Flutamide* acts by blocking translocation of the androgen receptor to the nucleus. Most effective when used in combination with surgical or pharmacologic castration.
- *Aminoglutethimide* acts by blocking the synthesis of adrenal steroid from cholesterol. It must be administered with glucocorticoid replacement. Used for medical adrenalectomy, 2nd line therapy in failure with tamoxifen.
- *Raloxifen* is a SERM. Has estrogen antagonist effect on breast & uterus.

→ Enzyme useful in cancer---*L-asparaginase*.

Hormonal agent	Role/category	Use
1. Glucocorticoids	Lympho-suppressive/lympholytic effect	Leukemia/Lymphoma, myeloma, MPDs
2. Estrogen high dose	-	Metastatic breast ca.
3. Tamoxifen	Anti-estrogen	TOC for most breast cancers, E ⁺ /P ⁺ breast cancers, progesterone resistant endometrial cancers
4. Progesterone	Inhibits endometrial cells proliferate ⁿ	Receptor+ ve (P ⁺) breast ca.
5. Flutamide	Testosterone Antagonist	Palliation of disseminated prostate carcinoma
6. Leuprolide	Medical castration	Unresectable prostate cancers, E ⁺ breast ca in pre-menopausal women,
7. Anastrozole	Aromatase inhibitor	Advanced E ⁺ /P ⁺ breast ca

SKIN CANCERS

Non-melanoma skin cancers (NM/C)

	Basal cell carcinoma (BCC)	Squamous CC (SqCC)
◦ Also k/as	Rodent ulcer	Epithelioma
◦ Incidence	80%, M/c skin cancer	20% of all skin cancers
◦ M/c site	Inner canthus of eye	Sun exposed area
◦ M/c lesion	Ulcerative type	Epithelial pearl (invasive cell nest of epidermal keratinocytes)
◦ Dissemination	Almost never spreads painless	To regional LN via lymphatics Painless
◦ progress	Very slow growing (M/c low grade malignancy of HN region)	Faster growing than BCC (More malignant than BCC)
◦ T/t :	Highly radiosensitive electrodesiccation / cautery	Surgical excision (TOC) R _T (for head, neck Ca)
◦ D/g	Edge biopsy	
◦ Risk factor	White races (unknown in blacks) UV-radiation Arsenic-exposure history	Single M/c cause - sunlight Zn, Mo, Vit A, B12, C deficiency postulated

Other non-melanoma cutaneous malignancies

Merkel cell carcinoma	---	Head & neck, Neural crest derived, highly aggressive (metastatic rate 75%)
Sebaceous Ca	---	Eyelid
Microcystic adenexal Ca	---	Face
Dermatofibrosarcoma protuberans	---	Trunk
Porocarcinoma	---	Extremities

Malignant Melanoma

- M/C type --- Superficial spreading
- Most malignant --- Nodular & acrolentiginous
- Least common, least malignant --- Lentigo maligna
- M/C site in female --- Lower part of leg
- In males --- Front/back of trunk (Torso)
- Worst prognosis --- Amelanotic

Superficial spreading (SSM)	Lentigo maligna melanoma (LMM)	Acral lentiginous melanoma (ALM)	Nodular melanoma	Amelanotic
M/c type	Least common least malignant	Poor p/g	Poor p/g	Worst p/g
In whites		No radial growth phase		Pinkish fleshy
Younger	In elderly 70+	60 yr	Younger	
Any part	Face (HMF)	In acral parts palm, soles & subungual region	Any part	

Prognostic factors

1. Stage at the time of presentation and tumour thickness are the most important prognostic factor
2. Breslow system (microscopic primary tumour depth) measures tumour invasion
3. Clark system divides into I-V levels based on anatomic level of invasion into skin

Metastasis

- Regional LN are m/c site of metastasis
- Through blood stream to lungs, liver (huge liver), brain secondaries are typically black

- Clinical findings suggesting melanoma are
↑ in size, irregular borders, colour change, ulceration

- High risk factors for melanoma (>50 fold ↑ risk)
 - Persistently changing mole
 - Atypical moles in patients with 2 family members with melanoma
 - Adulthood
 - >50 nevi in 50 mm diameter

T/t

- Surgery (wide excision + clearance of margin) is the TOC.
Margins recommended are--- in situ: 0.5 cm, invasive upto 1 mm thick : 1.0 cm thick, 1-4 mm thick : 2 cm; >4 mm thick 2.5-3.0 cm
- Melanoma of
 - Eye --- enucleation
 - Fingers / toes --- disarticulation
 - Anal canal --- APR
- Elective regional block dissection : Lymphatic mapping and sentinel node biopsy.
- For loco-regional recurrent cancer : Isolated limb perfusion using melphalan etc.
- Chemo using single agent **dacarbazine** is considered the standard t/t. Other effective drugs Melphalan
- Immunotherapy with BCG and IL-2, monoclonal antibodies IFNα 2a or 2b

→ Most specific marker for melanoma: HMB 45 (and S-100)

→ Cancer with most number of neurological complication is malignant melanoma

→ 90% melanoma start in a preexisting nevus (commonly junctional nevus) De novo in normal skin in 10% cases only.

→ Melanoma in retina has got better prognosis, as there are no lymphatics, spread is delayed.

Remember

- No incisional biopsy in melanoma
- No induration occurs in melanoma
- No role of radiotherapy
- Not known before puberty

Turban tumour (cylindroma of scalp)

- Rare tumour of scalp skin
- Locally malignant and slow growing

Marjolin's ulcer

- Well differentiated SqCC which occurs in chronic scars, e.g. burn scars, scars of venous ulcer

- No spread to LN, as there is no lymphatics in scars
- Painless
- T/t – wide excision

Keratoacanthoma (*Molluscum sebaceum*)

- It is an benign overgrowth and subsequent spontaneous regression of hair follicle seen in adults
- Self-healing, nodular lesion with central ulceration

- *Acrochordon (skin tags) are mesenchymal tumour of skin, flesh coloured to dark brown pedunculated lesion in neck, back, axilla & groin.*
- *Cock's peculiar tumour is infected sebaceous cyst.*
- *Brooke's tumour is a tumour of hair follicles.*
- *Dermatofibroma is seen in trunk/neck.*

Premalignant lesions of skin

- Bowen's disease of skin
Intradermal condition containing large clear cells
Erythroplasia of Queyrat is Bowen's disease occurring over glans penis
- Paget's disease of nipple
- Leukoderma
- Senile / solar keratosis – due to exposure to sunlight
- Radiodermatitis – Arsenic dermatitis
- Chronic scars – Marjolin ulcer
- **Xeroderma pigmentosum** – there is *defective DNA* excision repair mechanism. It turns into malignant melanoma
- Chronic lupus vulgaris
- Chronic irritation with tar, dyes, etc.

NEVI

- Junctional nevus – commonly turns malignant (melanoma in 90%)
- Blue nevus – seen in children over buttocks (mongolian spot hand, feet)
- Juvenile melanoma (Spitz nevus) – in children on face
- Hutchison's melanotic freckle – seen in elderly and turns into lentigo maligna melanoma

Cutaneous manifestations of internal malignancy (cancers a/w)

- Acanthosis nigricans ---- Gastric adenocarcinoma (60%), also a/w insulin receptor deficiency, Cushing's syndrome, acromegaly, hirsutism with hyperthecosis

- Necrolytic migratory ---- Glucagonoma erythema
- Superficial migratory ---- Pancreatic adenoma also thrombophlebitis lung Ca (Trousseau's sign)
- Sweet's syndrome ---- Myelogenous leukaemia
- Paget's disease of ---- Intraductal or infiltrating, nipple ductal Ca
- Leser-Trélat sign ---- gastric adeno Ca
- Acquired ichthyosis ---- HD, NHL, MM, MF

Malignancies involving nails are

- Sq CC
- Melanoma
- BCC

Kaposi sarcoma

- Endothelium derived (**vascular origin**) multifocal tumour.
- Lesion are initially asymptomatic macules which evolve into violaceous blue-brown plaques gradually, multiple rubbery blue nodules (resembling hemangioma) may appear.
- D/s that simulates K~ : bacillary angiomatosis d/to *Bartonella henselae*.
- Usually seen in lower extremities in front of tibia in elderly males in Non-AIDS cases.
- Virus a/w KS : HHV-8.

AIDS Related KS

- K~ is the M/c malignancy in AIDS patient & also it is the M/c cutaneous lesion.
- Occurs primarily in homosexual male & perianal area is often involved.
- KS in HIV individuals does not depends on CD4 +count & occurs uniformly at all CD4 + counts
- In AIDS M/c site is head & neck region. In head and neck region, palate is m/c site
- GIT and respiratory tract often involved.
- Nodules rapidly ulcerate (Not seen/ uncommon in i.v.dg abuser)
- T/t :
- Extremely radiosensitive & radiation is TOC for localized ds.
- IFN- 2 (may be given in conjunction with zidovudine)
- Chemo with vincristine & bleomycin (marrow sparing drugs)

BRAIN TUMOURS

Brain Tumours in Childhood

- Brain tumours are m/c solid tumours of children. Overall second m/c tumours of children after leukemia & lymphoma.
- 20% of pediatric CNS tumours are located in spinal cord and 80% in brain (of these 50% arise in posterior fossa and 50% in supratentorial compartment).

There are age related differences in primary location ---

<1st yr --- Supratentorial predominate.

1-10 yr --- Infratentorial predominate owing to high incidence of juvenile pilocytic astrocytoma & medulloblastoma.

> 10 yr --- Supratentorial again predominate with diffuse astrocytoma being most common.

- Overall M/c brain tumours are astrocytomas
Astrocytoma > PNET / Medulloblastoma > Ependymoma
(40%) (20%) (10%)
- Papilledema is a/w midline/infratentorial tumours
- Brainstem tumours are a/w gaze palsy, CN palsies and sometimes UMN deficit (hemiparesis, hyperreflexia and clonus)

→ Posterior fossa tumours are m/c brain tumours in children < 12 years of age.

→ M/c brain tumour in childhood & Brain tumour with best prognosis --- Cerebellar astrocytoma

→ M/c midline brain tumour in childhood --- Medulloblastoma (M/c midline infratentorial brain tumour)

→ Suprasellar calcification is seen in --- Craniopharyngioma

Craniopharyngioma

- M/C supratentorial tumour in children
- Marked tendency to show calcification (suprasellar calcification)
- Neoplasm is usually cystic & benign
C/f-- bitemporal hemianopias / U/L visual field defect, raised ICT, growth failure, DI, delayed puberty.

Medulloblastoma

- 2nd M/c brain tumour in children after glioma & M/c midline tumour.
- Occurs in posterior fossa.
- Frequently disseminates along CSF and perineural sheath, capable of metastasizing to extracranial site.
- Highly radiosensitive

In Adult

- M/c intracranial tumour --- Metastases
- M/c brain tumour --- Astrocytomas
- M/c benign brain tumour --- Meningioma
- M/c primary malignant tumour of brain --- Glioblastoma multiforme GBM)
- Most malignant/worst prognosis --- Glioblastoma multiforme
- Primary CNS tumours seeding neuraxis --- GBM, medulloblastoma, ependymoma Anaplastic astrocytoma (Brain tumours with CSF spread)
- M/c tumour in cerebral cortex --- Metastasis (from lung)
- M/c cancer involving nerve plexuses --- Metastatic colorectal cancer.
- Brain tumour arising from neuroglial cells --- Astrocytoma, Oligodendrogliomas, ependymoma

Brain tumours : locations

- Meningiomas --- Parasagittal
- Oligodendrogliomas --- Frontal lobes
- Ependymoma --- Fourth ventricle in children or filum terminale in adult and typically appears in lumbosacral region
- Metastasis from lungs --- Cerebral cortex

M/c CNS tumours in

- Cerebral cortex --- Metastases (usually from lung)
- Meninges --- Metastases
- Cerebellum --- Astrocytoma,
- Spinal cord --- Ependymoma

Brain tumours a/w Calcification

- Oligodendroglioma (m/c brain tumour a/w calcification in adults)
- Craniopharyngioma (m/c brain tumour a/w calcification in children)
- Meningioma (bracket calcification & hyperostosis)

Risk Factors for Primary Brain tumours

- AIDS
- Turcot's syndrome
- Neurofibromatosis

- Optic glioma & low grade astrocytomas are a/w NF-1 while acoustic neuroma & meningioma with NF-2
- Brain tumor a/w Parinaud's syndrome --- Pinealoma
- T/t of b/L schwannoma --- Brain stem implant

NERVE SHEATH TUMOURS

- o **Schwannoma :**
Arise from neural crest derived schwann cell & produce compression symptoms. A/w NF-2. Contain **Verocay bodies**. Antoni A & B pattern of growth is seen. T/t of b/L schwannoma is **brain stem implant**.
- o **Neurofibroma :**
Involve dermis & s/c fat. Plexiform multiple neurofibromas are found in NF-1 (neurofibromatosis -1). Malignant transformation rate is very low. Sx is done for cosmetic regions. M/c tumour spreading to neural sheath.
- o **Triton tumour :**
Rhabdomyoblastic differentiation in a malignant peripheral nerve sheath tumours.
- o **Epitheloid malignant schwannomas :**
Aggressive tumour with S-100 immunoreactivity.

SPINAL TUMOURS

They constitute 20% of all CNS tumours.

Intradural	Extradural
Extra-medullary	Extra-medullary
1. Neurilemoma (30%)	1. Metastatic tumours are m/c
2. Meningioma (26 %)	2. Sarcoma
	3. Meningioma
Intra-medullary	4. Neurofibroma
1. Ependymoma	5. Lipoma
	6. Chordoma

- M/c spinal tumours are --- Extradural metastases
- Overall M/c primary spinal cord tumours are --- Nerve sheath tumour / neurofibroma (Dumb bell tumour)
- M/c location or site of primary spinal tumours --- Intradural -extramedullary
- M/c intradural spinal tumours --- Neurofibroma
- M/c site of meningioma --- Thoracic region
- M/c intramedullary spinal tumour --- Ependymoma

EYE TUMOUR

RETINOBLASTOMA

- o M/c intraocular malignancy of childhood
- o AD inheritance with variable penetrance
- o B/L in 30% cases (B/L cases are genetically determined).
- o Arises from premature cells of photoreceptor layer
- o **Cl/f:**
 - Initial sign in majority of patients is a white pupillary reflex (leukokoria) k/as **amaurotic cat's eye**
 - 2nd most frequent sign is strabismus (esotropia)
 - Other features - pseudohypopyon, hyphema, sec. glaucoma, vitreous h'mge, proptosis.
- o **Histo :**
Pseudorosettes are +nt (Flexner - winter Steiner rosettes)
↑ LDH & CEA; Calcification
- o CT-scan is useful in determining extent of possible invasion of optic nerve
- o A/w inactivation of Rb suppressor gene on chromosome 13. Familial retinoblastomas are a/w **osteosarcoma**. Osteosarcoma c/b seen in patients who survived of retinoblastoma.
- o **T/t :**
Enucleation (optic nerve must be cut as far back as possible for histopathologic examination to exclude the extension along the nerve)
In B/L cases enucleation in eye with advanced tumour & R_T & C_T (with vincristine) in less affected eye.
- o ↑ IOT in retinoblastoma helps in differentiating it from pseudoglioma (IOT ↓)

- **Amaurotic cat's eye** is d/to white pupillary reflex, seen in retinoblastoma & pseudoglioma.
- **Amaurosis fugax** is different. Seen in retinal microembolization & hypoperfusion as in arterial thromboembolism., carotid artery d/s. There is transient mono-ocular V_n loss d/to cessation of blood flow to retina.

HEAD & NECK CANCERS

Tumours of head & neck region

- M/C tumour in India are of head neck region and upper aerodigestive tract.
- Most malignant tumour that dvp above the clavicle are SqCC (epidermoid carcinomas) originating from resp tract & stratified squamous epithelium of upper aerodigestive tract.
- SqCC of tonsil & the base of tongue have early & high rates of metastasis to neck & lesions of buccal mucosa (cheek) & palate have — low rates
- Late metastasis to LN is seen in - Ca-lip
- M/c combination for induction chemotherapy is cisplatin + 5-FU
- M/c site of metastasis in oral Ca - level II LN

Ca-oral cavity

Anatomic borders are mucosa of lip externally & anterior wall of tonsillar pillar posteriorly. It includes ---

- Lips (m/c site of oral cancer)
- Mobile tongue (2nd m/c site after lips)
- Buccal mucosa (5%)
- Gums (mandibular, maxillary Ca) 10-17%
- Floor of mouth (13-17%)
- Hard palate

Ca-lip

- M/c site of oral Ca
- Lower lip is involved in 95% & is usually SqCC (Sometime BCC may occur esp in upper lip)
- Starts at junction of skin & mucosa
- Local recurrence rate is low
- Nodal metastasis to submental / submandibular LN
- T/t : excision with clear margin
 - Defect upto 1/3rd of lower lip or 1/4 of upper lip are primarily closed
 - For larger defects - cross lip flaps.
 - or Abbey / Estlander flaps
 - Moh's microscopic surgery offers highest cure rates for lip tumours.

Ca Cheek (Buccal mucosa)

- Tobacco abuse is a/w most commonly with Ca of buccal mucosa. (↑risk in tobacco, pan chewer & sniff dipper)
- Most patient present late with nodal metastasis (in 56%)
- More common in males but *Verrucous Ca*, a variant of cheek ca presents as an exophytic mass, F > M, a/w HPV infection, multicentric.

- T/t surgical resection ± R_T (trismus occurs after both)
- Local recurrence high after T/t

Ca Tongue

- 2nd m/c site of oral Ca after lips.
- Tobacco chewing is the m/c cause. Submucosal fibrosis, alcohol are also predisposing factors.
- Common in lateral border.
- M/c type is SqCC.
- Nodals spread to ipsil/L submandibular/submental nodes → Jugulo-omohyoid LN. But jugulo-diaphragmatic LN may be involved in ca posterior tongue.

Ca Hard Palate

- Both benign & malignant neoplasm of minor salivary glands are more common in palate than SqCC
- In India however epidermoid Ca is common.
- Recognized late as it presents as painless ulcer.
- Metastasis to cervical LN (Occult)
- T/t surgical resection ± R_T

Giant cell Reparative Granuloma of Jaw

- Benign lesion of Jaw which resembles osteoclastoma of bone.
- Histologically it resembles giant cell epulis & brown tumour of hyperparathyroidism.
- R_x : Calcitonin, Curettage rarely necessary.

SALIVARY GLAND NEOPLASMS

- Salivary glands are of 2 types: Major & minor

	Major	Minor
1. Glands	Parotid, S/m, S/L	Palate, upper aero-digestive tract
2. M/c site for tumor	Parotid glands	Palate
2. Commonest neoplasm	Pleomorphic adenoma	Muco-epidermoid Ca, adenocystic Ca
3. Mostly	Malignant	Benign

Pleomorphic Adenoma (Mixed tumour)

- M/c benign tumour of major and minor salivary glands.
- R_T have no role in T/t.

Adenolymphoma (Warthin's tumour / Papillary cystadenoma)

- Benign salivary gland tumor that is exclusively located in the parotid.
- Cut section - papillary appearance
- Hot spot with Tc^{99} (all other S~ produces cold spot)

- M/c site for calculi in salivary glands -- Submandibular
- M/c site for Major salivary gland tumour -- Parotid
- M/c site for minor --- -- Palate (other sites - sinuses, upper aerodigestive tract)
- M/c salivary gland neoplasm overall -- Pleomorphic adenoma (mixed S~)
- M/c malignant S~ -- Muco-epidermoid Ca.
- M/c Radiation induced S~ -- Muco-epidermoid Ca
- M/c malignant S~ of minor -- Adenoid cystic ca.
- M/c salivary glands tumours in children are benign hemangiomas > lymphangiomas which are usually +nt in infancy

- Parotid Sx complication: Facial nerve (or any other CN) if injured it should be repaired immediately (**On table repair**) in OT.

Adenoid cystic ca

- Consist myoepithelial cells and duct epithelium cells
- Cribriform or lace like appearance
- Infiltrates via neural tissue
- M/c minor salivary gland tumour.
- Good prognosis.

THYROID CANCERS

T/t of Differentiated Thyroid cancers

- Surgical removal** is the TOC for thyroid carcinomas, Hemithyroidectomy --- for minimally invasive disease. Near total / Total thyroidectomy --- for maximally invasive papillary / follicular Ca.
- Medical T/t- Thyrotropin- α injection can stimulate uptake of I^{131} by thyroid cancer or residual thyroid.
- Radioiodine/ Sodium iodide (I^{131})** 30-50 mCi is administered to patient with an original papillary or follicular carcinoma > 1.5 cm in diameter & also in patient

having persistent radioiodine uptake in thyroid bed

- External Radiation to bony metastases. brain metastases are best treated with gamma knife radiation therapy.

Medullary carcinoma of thyroid (MTC)

- Arises from ultimobranial bodies (parafollicular C-cells)
- Contains amyloid stroma.
- Solid hard nodular tumour that **DOES NOT TAKE UP IODINE**.
- Secretes calcitonin (so calcitonin is tumour maker.) Levels of calcitonin fall after resection but rise again after recurrence, so best for follow up the patients
- Diarrhea occurs in 30% cases, involvement of LN in 50-60% cases.
- Tumours are familial in 10-20% cases.
- A/w pheochromocytoma and hyperparathyroidism in MEN type-2A

If a/w mucosal neuromas involving lips, tongue, inner aspect of the eyelids with marfanoid habitus, than syndrome is referred as MEN-2B

- Blood borne metastasis common.
- T/t. : Total thyroidectomy and resection of LN's (modified radical neck dissection). Medullary Ca is treated surgically, repeated neck dissection often required overtime. Patient found to have RET-proto-oncogene mutations are advised to have a prophylactic total thyroidectomy ideally at age of 6 yrs.

→ Before surgery measurement of catecholamines level should be done to exclude pheochromocytoma.

→ In anaplastic thyroid cancer, response depends on degree of anaplasia. Greater the anaplasia lesser the response

→ Radiation induced thyroid cancer is papillary carcinoma and thyroid cancer treated by external radiation is anaplastic thyroid cancer

→ Bone secondaries are m/c with the follicular type

→ Tumour marker to detect recurrence in post operative case of follicular carcinoma---Thyroglobulins

→ Calcitonin is a tumour marker for both medullary > follicular carcinoma.

→ Follicular carcinoma (FTC) is differentiated from follicular adenoma by --- Presence of normal appearing follicular cells and Vascular/capsular/lymphatic invasion.

→ Thyroglobulin or TTF-1 staining is essential to confirm thyroid origin of metastatic tumour

Points	Papillary	Follicular	Anaplastic	Medullary
1. Sp/F	M/c type (80%)	M/c in females	Most malignant	Uncommon
2. Mean age	42		57	—
3. Sex (F:M ratio)	2:1	3:1		—
4. Lymphatic spread	++++ (slow & late)	+	+++	++++ (earliest lymphatic spread)
5. Prognosis	Best		Worst	
5. Hematogenous spread	+	+++	++++	+++
6. Origin, a/w	Multifocal/ multicentric, Radiation induced, May arise in thyroglossal cyst	Common in region of iodine deficiency, A/w endemic goitre		Familial MTC are a/w MEN IIa & IIb
7. Patho	Orphan annie eyed nuclei+ (Ground glass appearance), Psammoma bodies	Resembles normal thyroid (FNAC is not helpful in differentiating it from adenoma)	Undifferentiated	Hyaline amyloid stroma
8. Cl/F	Most pts are euthyroid, Metastatic cervical node with occult primary	Usually presents as solitary nodule & recent change in long standing multinodular goitre		Secrete Calcitonin → ↑Ca ⁺⁺ (rare) 5-HT → carcinoid ACTH → cushing syndrome PG, VIP → Diarrhea Despite very high calcitonin level hypercalcaemia is very rare
8. Concentrate radioiodine (¹³¹ I)	Yes	Yes		No
T/t	Pt with minimal disease Lobectomy + isthmectomy • Near total thyroidectomy & follow up with thyroglobulin level • Post operative ¹³¹ I or RT • For nodal recurrence:MRND	Lobectomy + removal of isthmus & pyramidal lobe for adenoma but for carcinoma total thyroidectomy • Radioiodine	Ext. radiation p r o d u c e s d r a m a t i c s h r i n k a g e w h e n c o m b i n e d w i t h c h e m o	• Total thyroidectomy + removal of affected cervical nodes at the earliest age of D/g • External radiation + chemotherapy are palliative

- *Hurthle cell variant* is a variant of FTC (Follicular thyroid carcinoma). It is differentiated from FTC by following points.
 - Poorly differentiated
 - does not take I^{131}
 - bone metastasis is common

MEDIASTINAL TUMOUR

Thymoma

- Neoplasm of thymic epithelial cells or lymphocytes.
- M/c mediastinal tumour (25% of total).
- M/c site – anterior mediastinum (but c/b seen in superior mediastinum)
- 80% are benign and asymptomatic.
- Malignant thymomas are locally invasive and involve pericardium, great vessels, lung. Compression symptoms like SVC syndrome c/b seen.
- Pleural and pericardial dissemination occurs in stage IVa
- About 30% of patients with thymoma have MG, and about 15% of patients with MG develop thymoma
- Can produce variety of paraneoplastic syndromes
- **Important associations are**
 - Myasthenia gravis (30%) is m/c association
 - Pure red cell aplasia, Cytopenia
 - Acquired hypogammaglobulinemia
 - Autoimmune d/s (like RA, SLE, polymyositis)
 - Paraneoplastic syndromes (Cushing syndrome), Addison's d/s, agranulocytosis, alopecia areata, sarcoidosis, scleroderma.
- **T/t**
 - TOC for thymoma is total thymectomy
 - Neoadjuvant chemotherapy (platinum based) used for shrinkage of large bulky high grade thymomas
 - Neostigmine (\pm steroid) may be given to MG patient initially but early thymectomy is now recommended for all patients with symptomatic MG whether or not thymoma is suspected.
- **Prognosis after thymectomy**
 - About 75% of patients with MG are improved and 30% achieved complete remission
 - Younger patients benefit more than those >40 years
 - Females do better than male
 - Shorter duration of disease & absence of thymoma results in earlier remissions & improved results after thymectomy.

PARAGANGLIOMA

- Neoplasm of paraganglia (specialized neural crest cells).
- Tumours of adrenal medulla, chemoreceptors(carotid body and aortic body) vagal body and small group of cells a/w thoracic /abdominal or retroperitoneal ganglia.
- +ve for chromogranin, synaptophysin, NSE, CD56, CD57
- Microscopy shows dense core granules (Zellballen pattern)

BREAST CANCER

Risk Factors

- Age >50 year is the most important risk factor.
- Family history (first degree relatives; mother, sister).
- Excessive estrogen exposure
- Nulliparity.
- Risk is \uparrow ed by previous breast cancer, ovarian cancer, endometrial cancer, ductal carcinoma in situ, lobular carcinoma in situ, hyperplasia (unless mild), complex fibroadenoma, radial scar, papillomatosis, sclerosing adenosis, and microglandular adenosis. Risk is \downarrow ed by cervical cancer.

Gene	Chromosome	\uparrow Lifetime risk /Role in
BRCA-1	17p	Breast Ca (65%), 2nd breast ca (40-60%) Ovarian Ca (39%), Prostate
BRCA-2	13	Male breast cancer (6%) Female breast cancer (45%), Ovarian Ca (39%), Other - pancreatic/stomach etc

Prognostic factors

- Provided by tumour **staging**. Tumour size and axillary LN involvement are best prognostic indicators
- Other bad prognostic factors:
 - Absence of estrogen and progesterone receptors.
 - High S-phase fraction and thymidine labeling index.
 - Over expression of EDGF receptor, erB-2 gene or mutated p53 gene.
 - Over expression of HER-2/ neu in breast cancer is a/w poor prognosis and recurrence.
 - More microvessels in tumour.
 - Absence of metastatic suppressor gene nm23.
 - Aneuploidy.

- **Nottingham Histologic Score system** (the Elston-Ellis modification) is used for determining the grade of a breast cancer.

Work up of a breast mass

- FNAC is the 1st step in workup of a breast mass.
- IOC for breast cancer is → Two-view mammography (ie, craniocaudal and oblique) is the imaging method of choice for breast screening.
- MRI is the most sensitive imaging modality for DCIS.
- The ultimate diagnostic biopsy is open excision biopsy of a lesion
- **Pectoral group** of axillary LN are 1st to be involved in most cases
- M/c blood borne metastasis --- to spines.

Clinical /Pathological entities

- **Black star breast** : A radial scar is a star-shaped breast mass that may be completely benign, or it may be precancerous or contain a mixture of tissue, including hyperplasia, atypia, or cancer. Also k/as complex sclerosing lesion of the breast, black star, sclerosing papillary proliferation, infiltrating epitheliosis.
- **Fibroadenoma** is also termed as **breast mouse**. It is m/c breast tumour in a young women (<35 yr). **Popcorn calcification (Macrocalcification)** is seen in mammography.
- **Fibrocystic d/s of breast (FCD)** is m/c cause of breast mass in a women <50 yr. Incidence of cancer is high in a patient of FCD with **epithelial hyperplasia**.
- **Intraductal papilloma (Duct papilloma)** is m/c cause of blood stained nipple discharge. T/t is **microdochotomy**.

→ M/c breast mass in a woman <50 year → **Fibrocystic disease**.

→ M/c breast mass in a woman >50 year → **Infiltrating ductal carcinoma**

→ M/c breast tumor in a woman <35 years old → **Fibroadenoma**

→ M/c cause of blood stained nipple discharge in a woman <50 year → **Intraductal papilloma (Duct papilloma)**

→ M/c cause of blood stained nipple discharge in a woman >50 year → **Infiltrating ductal ca.**

Paget's d/s of Nipple

- Invasion of epidermis by malignant cells. Superficial manifestation of deep seated cancer.

- Eczematous lesion over nipple.
- Always a/w or begin with underlying intraductal carcinoma that extend to infiltrate the skin of nipple & areola.
- **Paget's cells** are large cells with clear cytoplasm, PAS +ve diastase resistant. These cells to be differentiated from superficial spreading melanoma.

Classification

(A) Non-Invasive In situ Carcinoma

Intraductal Ca or Ductal carcinoma in situ (DCIS)

- Begins with **epithelial hyperplasia** i.e. atypical hyperplasia of ductal epithelium (atypical ductal/lobular hyperplasia).
- Most sensitive investigation for ductal carcinoma in situ (DCIS) is MRI.

Lobular Ca in situ

- High incidence of developing cont/L breast cancer (30%).
- T/t excisional biopsy.
- Predominant Ca that presents concurrently with Fibroadenoma of breast.

(B) Invasive Carcinoma

Infiltrating (invasive) ductal Ca NOS

- Classic & most common breast Ca (accounts for 70%)
- Clinically majority of I~ have hard consistency d/to dense collagenous stroma (scirrhous carcinoma)
- Common site is left breast outer & upper quadrant with progressive infiltration of subdermal plexus & cooper's ligament there is extensive edema of skin -peau d'orange.

Infiltrating (invasive) lobular Ca

- Frequently B/L and within same breast it is multicentric in origin, t/t B/L total mastectomy is required.
- Characteristic "single file / indian file" linear arrangement

Medullary carcinoma

Fleshy or brain like consistency (encephaloid Ca~)

Adenoid cystic (invasive cribriform Ca)

Excellent p/g

- **Capecitabine** is oral 5-FU prodrug approved for t/t of resistant breast & colorectal cancer.

- Triple assesment for breast cancer include --- Cl/ E + Mammography + FNAC
- Cancer with eczematous changes of the nipple ---- Paget's disease.
- Cancer misdiagnosed as acute mastitis ---- inflammatory carcinoma.
- Cancer with increase incidence of bilaterality ---- lobular carcinoma in situ.
- M/c subtype of breast cancer with high propensity for CNS, ovary, uterus, bone marrow metastasis ---- invasive lobular carcinoma.
- Sentinel node biopsy is helpful in--- Breast cancer, Melanoma

Conservative Breast Sx

Indications:

Localized breast Cancer

- A. Optimal therapy for early breast cancer
- B. Stage I or II (localized tumor)
- C. Lymph node involvement is not a contraindication provided that LN must not be fixed to other LN/ surrounding tissue
- D. Invasive ductal and lobular cancer not contraindication
 1. Tumor must not be diffuse
 2. Requires that negative surgical margins are achieved

Absolute Contraindications

1. Two or more primary tumors in different quadrants
2. Associated **diffuse** suspicious microcalcifications
3. **Prior breast irradiation**
4. Pregnancy (unless near term)

Relative (cosmetic result related) contraindications

1. Collagen vascular disease (poor vascular supply)
2. Large tumor in small Breast

TUMOURS OF THE HEART

Myxoma

- M/c primary tumour of heart in adults.
- Left atrium is the m/c site.
- Often they arise from fossa ovalis region of atrial septum.
- Produce "ball valve" obstruction to outflow.
- 10% individual have "Carney complex". AD inheritance, skin pigmentation, other sites myxoma.

- M/c primary tumour of heart in adult is Lt atrial myxoma.
- M/c primary tumour of heart in children is rhabdomyoma

LUNG CANCERS

- Differentiating points b/w a benign and malignant lesion of lungs

	Benign (<5%)	Malignant (90%)
Change in size	Not ↑ed in size on CXR for ≥ 2 yrs	Age > 45 yr, recent ↑ in size
Calcification	Concentric/heavy	Small flecks like.
Volume doubling time is	> 500 d	< 30 d
Lesion size	< 1 cm	> 1cm
E.g.	Bronchial adenoma, Hamartomas	Bronchogenic Ca

- **Bronchial adenomas** are central (80%)/ endobronchial, slow growing lesions derived from neuroendocrine tissue (Mostly carcinoids) of major bronchi. Recurrent hemoptysis may be seen. Sx excision is TOC.
- **Hamartomas** are **peripheral** lesions of elderly derived from meso-endothelial tissue (Mostly carcinoids). Show popcorn calcification. Clinically silent.

- Most benign nodules of lungs are not true tumour. Mostly they are granulomas (TB or histoplasmosis)
- M/c cause of a solitary coin lesion in lung --- granulomatous disease (TB / histoplasmosis)
- M/c primary neuro-endocrine tumor of lung with a low grade malignancy --- Carcinoid tumour

Pancoast tumour (Superior sulcus tumour)

- Apical lung cancers which occurs in posterior superior chest in the superior pulmonary sulcus
- M/c histological type is SqCC.

- Invades
 - Cervical sympathetic plexus → **Horner's syndrome** (Enophthalmos, ptosis, miosis, ipsi/l anhidrosis)
 - Lower trunk of brachial plexus (C8, T1 & T2 nerves) → Severe radicular pain in the distribution of ulnar nerve
- R_x :- Radiotherapy & chemotherapy

Scar carcinoma

- Seen in infarcts (>50%) & tubercular scars (25%).
- Histologically it is an adeno-carcinoma
- Located in upper lobes.

Squamous cell Lung carcinoma (SqCLC)

- M/c lung cancer in **smokers**.
- Produces PTH, PTHrP → *Hypercalcemia*
- Remember 5 'c' of SqCLC :
A/w Cigarette smoking, central, cytology detection, clubbing+, Calcium high, cavitating .

Adeno carcinoma (SqCLC)

- M/c lung cancer in **non-smokers & in females**.
- Pulmonary symptoms are late as it is very slow growing.
- DIC is common.

Bronchoalveolar carcinoma

- A variety of adenoca derived from **clara cells**(non-ciliated epithelium)
- Lobar pneumonia like picture
- Lung to lung metastasis +nt.
- Prognosis is very good.

Small cell/Oat cell Lung carcinoma (SCLC)

- M/c lung cancer producing paraneoplastic syndromes d/to variety of ectopic hormone production:
 - ACTH → Cushing syndrome
 - Calcitonin → *Hypocalcemia*
 - ADH (vasopressin) → SIADH (Hyponatremia)
 - Anti Ca^{++} channel antibodies → Lambert-Eaton Myasthenic syndrome

Large cell carcinoma (LCLC)

- M/c lung cancer causing gynaecomastia .
- Hypertrophic pulmonary osteoarthropathy (HPOA) is common.

Type	Squamous	Adeno	SCLC (small/oat cell type)	Large cell
M/c in	Smokers, India	Overall, & in female		
M/c lung cancer causing	Pancoast tumour	Late symptom	SVC syndrome, ectopic hormone produc ⁿ	Gynaecomastia, HPOA
Growth	Slow	Slow	Rapid	
Prognosis	Best	Good	Worst	Good
Malignant behaviour	±	+	+++	
Metastasis	Least	Late	Most common	
Clubbing	+			++
Cavitation	++			+
Sputum cytology	+ve			
Staining	Deep eosinophilic		Small basophilic	
Location	Central	Peripheral	Central (Perihilar)	
T/t	Sx		Chemo ± RT	

→ M/c lung cancer overall is → Metastasis from breast cancer (adeno ca. is m/c primary lung ca.)

→ M/c lung cancer and m/c histologic type → Adeno but SqCC in India

→ Mc site of metastasis from lung is → lung > Liver > Adrenals.

→ Most tumours / malignancies are a/w hypercalcemia but in tumour lysis syndrome there is hypocalcemia.

→ SqCC & SCLC both are centrally located, both are strongly a/w smoking & both are cause of SVC syndrome

→ PTH rP is a/w hypercalcemia.

PTH rP is secreted by → SqCC of lung, Adenocarcinoma kidney, Metastasis from breast ca.

→ M/c symptom of primary lung Ca. → Cough and m/c symptom of lung metastasis → dyspnea.

→ Hormones produced by SCLC → ACTH, AVP/ ADH (Vasopressin) calcitonin, ANF, Gastrin rP

→ Most radiosensitive lung cancer → SCLC

GIT, LIVER & PANCREAS

Ca - ESOPHAGUS

- Common in 50-70 yr. male
- Risk factors
 - Smoking, alcohol
 - Dietary deficiencies of (Vit A, C and riboflavin) Mo, Zn
 - Esophageal web with glossitis and iron deficiency (Plummer Vinson/Paterson-Kelly syndrome) – in females
 - Chronic achalasia
 - Strictures (Lye, hot tea), Tylosis
 - ↑ Consumption of nitrates, mycotoxins
 - GER and Barrett's esophagus (adeno ca)
- Pathology:
 - SqCC in upper 2/3rd
 - Adeno ca in lower 1/3rd
 - (15% in upper 1/3 + 35% middle 1/3rd).
 - Overall m/c histological type now a days is adenocarcinoma and m/c location in west is lower 1/3rd.
 - In India m/c histology--- SqCC located in middle esophagus.
- Symptoms: Stickiness behind sternum while taking food is the earliest symptom. Dysphagia usually to solids, is a late but m/c symptom/presentation.
- Spread – commonly to Lt supraclavicular LNs, liver, lungs and pleura LN involvement, esp to coeliac is bad prognostic factor
- Ba swallow : Shouldering sign and irregular filling defect
- IOC - Endoscopic (transluminal/transesophageal) USG is best as it depicts depth of involvement (T-stage)
- Esophagoscopy biopsy – is diagnostic.
- Best scan for abdominal metastases : FDG-PET scan
- T/t
 - For upper 2/3rd → Radiotherapy is TOC
 - For middle 1/3rd → Sx
 - For Lower 1/3rd → Sx
- M/c Sx is Ivor Lewis operation:
 - Laparotomy & thoracotomy → Subtotal esophagectomy with reconstruction. M/c cause of death in Ivor-Lewis is **anastomotic leak**. After esophagectomy esophagus is replaced by stomach.
- In advanced cancer only palliation is possible

→ Postcricoid tumour is treated mainly by radiotherapy.

→ Safe margins for cancers:

1. Esophagus 10 cm
2. Stomach 5 cm
3. rectum 2 cm

Ca - STOMACH

- Risk factors:
 1. Long term nitrates ingestion (dried, smoked, salted foods) → Achlorhydria : so more common in China.
 2. Pernicious anemia → Fundal carcinoma
 3. Partial gastrectomy
 4. Premalignant conditions
 - Ménétriér's d/s
 - Adenomatous polyps
 - Atrophic gastritis
 - Intestinal metaplasia type3
 - H.pylori infestation
 5. Blood group A,
- No association is seen b/n gastric Ca & duodenal ulcer
- Cl/f ---
 1. Dysphagia is seen in lesions of cardia
 2. Metastasis to
 - Left supraclavicular LN → Virchow's nodes / trovier's sign
 - Ovary → Krukenberg's tumour
 - Periumbilical region → Sister Mary Joseph node
 - Pouch of Douglas or cul de sac/drop metastasis → Rectal shelf of Blumer's palpable on PR or PV/E
- M/c site of metastasis: - Liver
- Unusual features : migratory thrombophlebitis, microangiopathic hemolytic anemia, acanthosis nigricans (Black lesion in axilla), Leser-Trélat sign (multiple outcroppings of seborrheic keratosis)
- Borchardt's triad:
 - Upper GI fullness and pain +
 - Retching without vomiting +
 - Inability to pass Ryle's tube.
- Linitis plastica also k/as Brinton's d/s or leather bottle stomach, is a morphological variant of diffuse (or infiltrating) stomach cancer. Seen in adenocarcinoma of stomach.
- Surgery is the TOC. Total gastrectomy for proximal Ca.
- To diagnose liver secondaries from gastric cancer best investigation is CECT or MRI

- M/c benign tumour of stomach is --- Adenoma (Earlier it was leiomyoma)
- M/c tumour of small intestine --- lymphoma
- M/c extra nodal site of lymphoma --- Stomach
- M/c site of gastric carcinoma in pernicious anemia --- Fundal

ZES (Zollinger Elision Syndrome)

Drug of choice for ZES is PPI (proton pump inhibitor). Use of PPIs decreases the need for total gastrectomy. Dose of PPIs is higher initially.

Type-I (G-cell hyperplasia)

G-cell (non-beta islet cell) hyperplasia with hypergastrinemia and chronic peptic ulceration. Treatment is partial gastrectomy with removal of β cell area.

Type-II (Gastrinoma)

- 2/3rd are malignant.
- M/c site is duodenum /gastrinoma Δ k/as Psaro's triangle, which is f/by junction of cystic duct and CBD, junction of neck and body of pancreas, junction of 2nd and 3rd part of duodenum). Tumours which are outside the gastrinoma Δ have worst prognosis.
- M/c cause of ZES
- Secrete gastrin (in 70%). Located in pancreas in 85% and 25% are a/w MEN-1.
- ZE triad:
High gastrin + high acid + Non- β cell tumour of pancreas
- Triad of symptoms:
Peptic ulceration + diarrhoea + gastric acid hypersecretion

Peptic ulcers is usually a solitary duodenal ulcer (m/c type of PUD)

- If PUD is a/w diarrhoea, MEN1, unusual location, multiple lesion, refractory to t/t or without H. pylori infection it suggests a d/g of ZES
- Screening test: \uparrow BAO (BAO:MAO ratio $>0.6:1$)
Fasting serum gastrin >1000 pg/ml
Confirmatory/ provocative test --- I/v secretin test (paradoxical \uparrow in already increased serum gastrin level)
- T/t: Surgical removal is TOC (Streptozocin - most effective dg)

Insulinoma

- M/c pancreatic endocrinal tumour (β - cell tumour).

- Single, equally distributed, encapsulated tumour.
- Whipple's triad :

Fasting hypoglycemia (< 50 mg%) +

Symptoms of hypoglycemia +

Immediate relief after glucose administration.

- **Weight gain** is seen.
- Most reliable test for d/g --- 72hr fasting serum glucose value. C-peptide, and insulin measurement every 4-8 hours. Plasma insulin levels are elevated at the time of hypoglycemia.
- Insulin /RBS ratio >0.3
- T/t : 75-95% of patient respond well to surgery. Before surgery hypoglycemia is controlled by use of **diazoxide**

GIST

- Gastrointestinal stromal tumours.
- Arise from intestinal *cells of Cajal*.
- M/c site stomach (45-60%), small bowel (30%), esophagus & rectum (10%).
- Metastasis to liver, omentum, peritoneum. Lymphadenopathy is unusual.
- C-kit proto-oncogenes are involved, which act thru tyrosine kinase. Overexpression of **CD117**.
- Dx: PET scan is gold standard for Dx of GIST.
- Rx: Excision \rightarrow if recurrence \rightarrow **Sunitinib/ imatinib**.

VIPoma

- \uparrow Colonic motility.
- A/w WDHA syndrome (Watery/secretory Diarrhoea, Achlorhydria).
- Inv: Somatostatin receptor scintigraphy.

CARCINOIDS

- Overall GIT is the m/c site f/b lungs. In GIT ileum is the commonest site.
- For the 4 most common sites of occurrence the **incidence of metastases** varies greatly. Jejunum or ileum (70%) $>$ Appendix 35% $>$ Lung or bronchus (27%) $>$ Rectum (14%).
- Small intestinal carcinoids are the most frequent cause of carcinoid syndrome due to metastasis in liver.
- Appendiceal carcinoids occur at early age (40 yr), usually <1 cm size and do not metastasize.

Carcinoid syndrome

- Results from extensive hepatic metastasis.
- Heart is involved in 50% of cases mainly **endocardium** and **valves of right side of the heart** and presents mainly as TR

+ **PS (tricuspid regurgitation and pulmonary stenosis)**. Involvement of the tricuspid valve is c/by deposition of fibrous plaques on the leaflets and ventricular attachments. Left sided lesions are found in patient on methylsergide or ergotamine.

- Presents as flushing of the skin, cramps, nausea, vomiting and diarrhea d/to serotonin, kallikrein, bradykinin, histamine, PG's etc.

→ Carcinoids of lung are also common.

→ M/c tumour of small intestine ---- lymphoma

→ M/c extra nodal site of lymphoma --- Stomach

→ M/c site of gastric carcinoma in pernicious anemia --- Fundal

GI/COLONIC POLYPS

Class	Subtypes	Example, Feature	M/c site	Risk
Non-Neoplastic	Inflammatory	Solitary rectal ulcer syndrome	Rectum	0%
	Hamartomas	Peutz-Jegher's	Jejunum, ileum	0%
		Juvenile	Rectum	0%
	Hyperplastic			0%
	Lymphoid aggregates			0%
	Pseudopolyp	UC		0.1%
Neoplastic (Adenomatous polyps)	Adenomatous	M/c neoplastic polyp		5%
	Tubular	0-25% villous tissue		
	Tubulo-villous	25-50 % villous tissue		20%
	Villous	75-100 % villous tissue, sessile, K ⁺ rich discharge		20%
	Classic FAP	>100 polyp		100%
	HNPCC	Lynch syndrome	Colon	

ca pancreas, lung, uterus, breast, ovary (*sex cord tumors*) is there.

- *Juvenile polyps* are m/c colonic polyps in children. non-neoplastic. Usually do not transform into colon cancer but associated risk of ca pancreas, lung, uterus, breast, ovary (*sex cord tumors*) is there.
- *Inflammatory & pseudopolyps* Colonic cancer is rarely seen in long standing cases of UC which arises in the region of epithelial dysplasia and not from polyps.
- *Adenomatous polyps* are m/c neoplastic polyps. They **ave malignant potential**. Only adenomatous polyps are clearly premalignant. Malignant potential of adenomas correlates with type of polyp, size, and degree of dysplasia. Higher grades of dysplasia, ↑ing % of villous tissue within the polyp, and polyps >1 cm in diameter are a/w ↑ed risk of malignancy. A polyp is considered malignant when cancer cells within the neoplasm have extended to the submucosa via penetration through the muscularis mucosal layer.

Examples are :

- Tubular adenomas (most common) : Pedunculated
- Tubulo- villous adenomas
- Villous adenomas : Sessile
- *Factors that place patients at higher risk of developing metachronous adenomas* [5 'M']
 - Male gender,
 - Multiple polyps,
 - More than 2 cm,
 - Morpho/ histology : polyps with tubulovillous and villous histology at index polypectomy,
 - Member of family with history of colorectal cancer

Familial adenomatous polyps/ FAP or FPC

- Presence of > 100 neoplastic polyps / adenomas (average no. is about 1000) on colon mucosa.
- AD inheritance.
- Due to germline mutation in APC tumour suppressor gene located on chromosome 5q.
- Flexible sigmoidoscopy of first degree relatives of FAP pt beginning at the age of 10-15 year is the mainstay of screening method.
- If FPC is not treated by surgical resection, Colorectal cancer develops virtually in 100% of cases before the age of 40.
- **Total colectomy** is required as soon as diagnosis is made

Gardner's syndrome

FPC + extra colonic lesion [e.g. **Multiple osteomas**, desmoid tumours, sebaceous (epidermoid) cyst, lipomas & other connective tissue tumours], may be a/w MEN II b

- *PJS (Peutz Jegher's syndrome)* is intestinal polyposis + melanotic hyperpigmentation around oral cavity. Usually do not transform into colon cancer but associated risk of

- *Turcot Syndrome*
FPC + brain tumors
- *Lynch syndrome (HNPCC, non-polyposis syndrome)*
Adenoma of proximal colon + endometrial + ovarian ca.
HNPCC is a AD trait a/w mutations of **hMSH2** on chromosome 2 and **hMLH1** on chromosome 3. The most frequent extra-colonic primary sites among the HNPCC families were: endometrium (26.5%) and breast (26.5%) (women), and stomach (35.1%) (men).

Carcinoma colon

- Adenocarcinoma is **m/c** form
- Sigmoid colon (21%) is commonest site after rectum (38%).
Rectum is the **m/c** site of colorectal cancer (38%).
- Increase risk with FAP (100% risk), Gardner/ Turcot's syndrome, long standing UC and CD.
Red meat, saturated fat, cholesterol, alcohol, smoking, increases risk
High fibre diet, aspirin/NSAIDS have protective role
- Genes involved are --- K-ras mutation, APC, mismatch repair genes
- Types ---
Annular/stenosing type is more common on Lt. side and often presents with intestinal obstruction/ alteration of bowel habits (d/to mural involvement).
Ulcerative type is common on Rt. side, Rt sided growth commonly present with anemia, palpable mass.
- Carcinoma caecum occasionally presents like acute appendicitis, intussusception.
- *Metastasis*
Liver is the **m/c** site of metastasis (40%) via portal vein i. e. hematogenous. Solitary secondaries of liver may be resected surgically.
- Fecal strength of streptococcus bovis increased many folds.
- **I/gⁿ**
Colonoscopy
Ba-enema → 'apple-core' deformity
CEA is specific tumour marker which is primarily associated with C~ (rise in CEA indicates recurrence or secondaries)
- T/t : mainly surgical
 1. Rt. sided growth --- Rt. radical hemicolectomy with ileotransverse anastomosis.
 2. Lt. sided --- Lt. radical hemicolectomy
 3. Solitary secondaries of liver, are resected surgically by segmental resection

4. Chemotherapy using 5-FU + folinic acid.

Adjuvant chemotherapy is useful in Dukes stage B and C.

- **Prognosis** : depends on
 - Site (Left tumours has got better p/g)
 - Type (colloidal better than mucinous)
 - Size and LN status
 - Liver secondaries has poor prognosis

Ca ANAL CANAL

- M/c it is SqCC.
- TOC for anal canal ca above dentate line - **Chemoradiation.**
- TOC for anal canal ca below dentate line - WLE
- If recurrence is there Abdomino perineal resection.

Ca HEAD OF PANCREAS

- A/w smoking, chronic pancreatitis (Point mutation of p53 & ras oncogenes)
- Ca head of pancreas, Periapillary Ca & pancreatitis - Ba- meals will show *widening of C- loop of duodenum (antral pad sign) + Inverted 3 sign of frost berg*
- CECT scan are confirmatory (most specific)
- Contrast enhanced spiral CT is best initial investigation.
- Most sensitive test for Ca-pancreas is ERCP.
- Gold standard tumor marker ---- Elevated **CA 19-9**
- **Hypotonic duodenography** will reveals a 'rose thorn' appearance
- Resectable tumour of head / periapillary region are removed by Whipple's procedure [pancreaticoduodenectomy]
 - *Pancreatic cancer with best prognosis → Ca head of pancreas.*
 - *Prognosis is poor in body & tail cancers .*

LIVER CANCERS

Association with OCP

- *Cavernous hemangiomas*
M/c benign tumour of liver. Tend to enlarge with OCP (oral contraceptive pills) use or during pregnancy.

- *Focal nodular hyperplasia (FNH)*
NOT a/w OCP use but OCP use ↑es risk of hemorrhage.
- *Hepatic/hepatocellular adenoma*
Most strongly a/w long term OCP use & hypertension. Age & sex predilection is seen for young female.

Hepatocellular cancer (HCC)

- **Risk factors:** Hepatitis B and C, aflatoxins, alcohol, Cirrhosis from any cause (alcoholic/PBC), hemochromatosis, alpha 1 antitrypsin deficiency, Wilson's d/s, GSD, Citrullinemia
- **Cl/f:** Hepatomegaly is most common sign.
- Paraneoplastic syndromes: **Hypoglycemia**, erythrocytosis, hypercholesterolemia
- Tumour marker: AFP. other new markers are DCP / PIVKA-2
- **Cl/f:** Hepatomegaly is most common sign.

Angiosarcoma

- Highly aggressive tumour which arises from sinusoids of liver
- Carcinogens implicated in causation---Vinyl chloride, arsenic & thorotrast.

- Liver is the second only to LN as a site of metastases for tumours.
- Metastatic neoplasm represent the m/c malignant tumours of liver
- M/c neoplasm of spleen are lymphoma (but usually they are secondary)
- Hemangiomas are m/c benign tumour of liver and spleen
- Hamartomas are m/c benign tumour of lungs

Fibrolamellar Ca of liver

- Occur in young females without underlying cirrhosis.
- Slow growing, grossly encapsulated & well circumscribed.
- AFP is not elevated & prognosis is excellent.

GALL BLADDER AND BILE DUCTS

Carcinoma GB

- Mostly seen in 70 + females.
- Most patients have Hx of antecedent gall stones (>90%) but very few (0.2%) develop cancer.

- Risk factors:
 - Gall stones/ Cholelithiasis (0.2% risk) : M/c risk factor
 - Mirizzi syndrome
 - GB polyp
 - Porcelain GB (25% risk)
 - Ulcerative colitis
 - Choledochal cyst
 - Clonorchis sinensis
- **M/c type adenocarcinoma scirrhus type.**
- **R_x:** If diagnosis is made during cholecystectomy resection of a portion of liver alongwith GB is advocated.
- Secondaries in liver are common
- Symptomatic only in late stages
- **M/c site for adenocarcinoma GB is fundus and neck.**

- Chronic inflammation of GB can lead to calcium deposition in GB k/as porcelain gall bladder.
- Gall stones are m/c risk factor for Ca GB.

Cholangiocarcinoma (Bile duct cancer)

- Rare malignancy of the bile duct.
- M/c site : perihilar (2/3rd) i.e. at the bifurcation of hepatic ducts.
- Arises from biliary epithelium (cells having cytoplasmic mucin)
- A/w contrast agent thorotrast, Biliary tract infection with Clonorchis sinensis, chronic typhoid carriers, Caroli d/s, cholangitis (sclerosing), choledochal cyst, colitis (ulcerative),
- Not a/w cirrhosis of liver and cholelithiasis. (Cholelithiasis is not clearly a risk factor for cholangiocarcinoma)
- M/c type (95%) is adenocarcinoma of scirrhus type.
- Stones < 30%, M > F, 2/3rd are located at the hepatic duct bifurcation.
- **Cl/f:** Obstructive jaundice (>90%), biliary pain, cholangitis, biliary stasis, bile duct stones, infection.
- **T/t:** Surgical resection offers only chance of cure.
- Tumour of lower end of CBD : resectable by **whipple's procedure** (head and neck of pancreas + CBD and some part of duodenum resected, but portal vein is NOT resected).

KLATSKIN TUMOUR

- Nodular type of cholangio-carcinoma
- Lesions often arise at bifurcation (hilar) of CBD

- Usually a/w collapsed or shrunk GB (*exception to Courvoisier's. law*)
- Proximal hepatic ducts can be visualized by cholangiography

TUMOURS OF KIDNEY & URINARY TRACT

WILM'S TUMOUR

- Also k/as Nephroblastoma
- M/c renal neoplasm of childhood
- Imp. associations :
WAGR syndrome :
 (Wilm's + Aniridia + Genitourinary anomalies + Retardation, mental)
Beckwith- Wiedemann syndrome :
 (Wilm's + hemihypertrophy + organomegaly + omphalocele + macroglossia)
Dany's Drash syndrome :
- Polycythemia may occur becoz of erythropoietin production by tumour.
- Risk of WT increases by +nce of nephroblastomatoses (hyperplastic, perilobar & multifocal superficial types).
- P/g : Abnormal persistence of embryonal renal tissue (nephrogenic rests or nodular blastema or nephroblastomatosis) is related to favourable prognosis in b/L wilm's tumour. Brief course chemotherapy is beneficial.

RCC (Renal Cell Carcinoma)

- Also k/as hypernephroma/ Grawitz tumour.
- M/c malignant tumour of kidney.
- Imp. associations :
 - Smoking - strongest association
 - Von Hippel Lindau d/s
 - Adult PKD
- *Papillary (chromophilic) variant* is a/w trisomy 7,17 and loss of Y. There is a tendency to invade renal vein, a continuous cord of tumour cells in IVC & psammoma bodies are seen.
- M/c presentation is presence of painless hematuria with ballotable flank mass in elderly.
- Polycythemia, erythrocytosis, hypercalcemia, hypertension, Stauffer's syndrome may occur becoz of erythropoietin production by tumour..
- Bosnaik renal cyst criteria are CT criteria useful in differentiating renal cyst from RCC.

- T/t :Surgery
- **Transitional cell carcinoma of kidney** almost always involves a nephroureterectomy, which involves removing the entire kidney and ureter.

	Wilm's	RCC
Also k/as	Nephroblastoma	Hypernephroma/ Grawitz tumour
M/c renal tumor	In children	In adults
Oncogenesis	Loss of activation of WT-1 suppressor gene on chromosome 11p	AD inheritance in some cases
A/w	WAGR syndrome, Beckwith-Wiedemann, Dany's Drash syndrome	Smoking, obesity VHL syndrome Adult PKD Tuberous sclerosis
M/c Presentation	Asymptomatic abdominal mass	
Triad	Abd. mass + Hematuria + Fever	Flank mass + Hematuria + flank pain
Origin	Multicentric	Epithelial cells of PCT, upper lobe
Histo	Mixed tumour	Clear cell adenoca
M/c site of metastasis	lung	lungs Cannon ball deposits & Pulsatile secondaries are seen.
T/t	Nephrectomy, RT useful	No role of RT or chemotherapy

Nephroblastomatosis (Nephrogenic rests)

- ↑ Risk of wilm's tumour in contralateral kidney.
- Present in 100% of bilateral tumours.
- *Multicystic renal dysplasia* --- M/c cause of renal mass in infant (>50%)
- *Mesoblastic nephroma* --- M/c intrarenal tumor seen in newborn or < 2 months
- *Neuroblastoma* --- M/c abdominal malignancy in neonate and also in infants.
- *Nephroblastoma (Wilm's)* --- 2nd M/c abdominal neoplasm in children 1-5 yrs.

NEUROBLASTOMA

- Accounts for about 8% of childhood cancers and is the *m/c solid tumor of childhood outside of the CNS*.
- Most frequently diagnosed neoplasm in infants.
- A/w amplification of N-myc protooncogene on chromosome 1p and it is related to bad prognosis.
- Most N~ arises either in the adrenal gland or in retroperitoneal sympathetic ganglia (75%).
- Infants have localized disease usually in the cervical or thoracic region.
Older children - usually have abdominal N~ and disseminated ds.
- Abdominal N~ present as fixed (**non mobile**) hard abdominal mass that is producing discomfort/ dragging pain. (Remember WT is mobile)
- Eye signs -
 - Opsoclonus myoclonus* is rare but characteristic.
 - An affected child may present with chaotic eye movements, myoclonus and ataxia (*dancing eyes, dancing feet syndrome*).
 - Orbital proptosis and periorbital ecchymoses.
- D/g
 - Investigation of choice is CT or MRI
 - ↑ **VMA & HVA in urine** + Neuroblasts observed in bone marrow confirms the D/g.
 - Bone scan is used for evaluation of metastasis.
- Histology
 - Small blue round cell tumour
 - Calcification seen.
 - Homer Wright rosettes** (Ring of cells around a mass of central pink neural filament)
- Metastasis - Bone is the *m/c* site..
- Prognosis -
 - Depends upon age at the time of diagnosis, extent of tumor, n-myc amplification and chromosome 1p deletions in the tumour. Children < 1 yr. & 1 & 2 stages, thoracic and head neck types do well.
 - Prognosis is worse with N-myc amplification, chromosome 1 deletion (loss of heterozygosity for chromosome 1p), unbalanced 11q, and diploid tumours.
- T/t
 - Surgery is the TOC in early stages
 - Chemotherapy and radiation is required advanced disease (Stage-3+)
 - MIBG is under evaluation for radionuclide in N~.
 - Stage 4S: Localized primary tumor, with dissemination limited to skin, liver, and/or bone marrow. Treated by intensive chemotherapy.

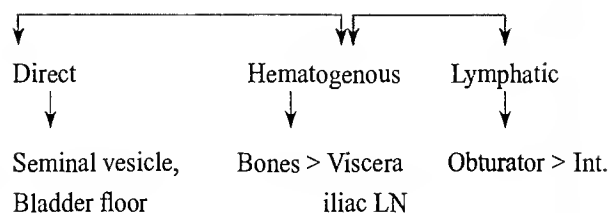
BLADDER CANCER

- ↑ *Risk of transitional cell Ca* is seen with
 - Balkan nephropathy (a/w se & Zn deficiency)
 - Analgesic nephropathy (Transitional CC of renal pelvis is also associated)
 - β - naphthylamine
- ↑ *Risk of adeno. Ca of bladder* is seen with
 - Cystitis cystica
 - Cong. urinary fistula
 - Ectopia vesicac / urachus remnants
- Risk of squamous cell Ca* is seen with
 - Schistosoma hematobium (Bilharziasis) in 70 % of patients
 - Vesical calculus may lead to → chronic irritation → SqCC
- *Schistosomiasis (Bilharziasis)* ↑ the risk of both SqCC and transitional cell carcinoma, but risk of SqCC is ↑ed many folds.
- *Boca virus* is a/w ↑ risk of bladder cancer.
→ *Transitional cell carcinoma* is the most common bladder cancer
- *Angioma* is least common tumour of bladder
- *Bladder Ca* is M/C at lateral walls & least at vault (but starts at vault)
- *M/c carcinoma of kidney* is adenocarcinoma & SqCC is least
- *M/c tumours of urethra* are → SqCC
- *M/c site of urethral carcinoma* → bulbomembranous urethra

PROSTATE CANCER

- Incidence of prostate cancer is highest among men, worldwide (prostate > Lung > Colorectal)
- M/c cancer with perineural invasion
- Commonly located in peripheral zone (posterior lobe is enlarged in cancer, while median lobe in BPH).
- Grading system used for P~ : Gleason's system
- Risk factors : Smoking, occupational exposure to rubber / Cadmium / Pesticides.
- Most effective method (screening method) for early detection of cancer is : **DRE + PSA**
PSA is also useful in follow up studies.
- Confirmatory investigation : transrectal USG with needle biopsy.

- Metastasis



Bones : Pelvis > Lumbar vertebrae > Thoracic vertebrae

Viscera : Lung > Liver > Adrenal

- T/t :

DOC is anti-androgens , GnRH agonists (Bicalutamide).
gold is also implicated in t/t of prostate cancer.

Stage	Feature	T/t
• A ₁		Observation only
• A ₂ or B	Palpable gland /organ limited	Radical prostatectomy
• C	Locally advanced	Irradiation
• D ₁	+ve pelvic LN	Irradiation + androgen deprivation
• D ₂	Distant metastasis	Androgen deprivation

TESTICULAR CANCER

- GCT (Germ cell tumours) are M/C histological type & occur between 20-40 years.
- M/c histological variety of T~ is ---- seminoma.
- M/c cause of a painless mass in the testicle ---- malignancy, most commonly a seminoma.
- M/c T~ in elderly (>50 year) : Lymphoma
- Risk factors for higher risk of GCT ---- Cryptorchidism, Testicular feminization synd., Klinefelter's synd.
- M/c B/L testicular malignancy ---- metastatic malignant lymphoma.
- Trans -scrotal biopsy is contraindicated.
- Markers:
AFP is never elevated in seminoma while hCG is occasionally elevated in seminoma.
LDH may be elevated in either type of tumour
AFP is ↑ed in - Endodermal sinus tumour
PAP - ↑ed in dysgerminoma and other GCTs.

Seminoma	Non Seminoma
• Accounts 50% of all GCT	• Contain derivatives from >1 germ layers
• ↑β-hCG	• ↑AFP + ↑β-hCG
• Responds best to radiation & have a best prognosis	• Responds to chemo
• Localized to testis for long time	• Early dissemination
• Presents in stage I	• Presents in stage II & III
• Mainly lymphatic spread	• Hematogenous spread may occur
• T/t :- Low stage ds : Orchiectomy+irradiation of the para-aortic LN High stage ds : Chemotherapy	• T/t :- Low stage ds : Orchiectomy + observation High stage ds : Platinum based chemotherapy + RPLND

- Screening method of choice for T~ is ----- USG (orchiectomy for confirmation of D/g).

Chorio carcinoma in males

- M/C testicular cancer producing gynecomastia
- Highly aggressive cancer (secretes β-hCG)

Teratocarcinoma

- M/c testicular cancer in adults containing derivatives from >1 germ layer.
- Mixture of embryonal carcinoma and teratoma (secretes both AFP / β-hCG)
 - First LN involved in right testicular tumour is interaortocaval LN just below the renal vessels.
 - For left testicular tumour paraaortic LN are 1st to get involved.
 - M/c tumour of epididymis is adenomatoid tumour which is benign.

PENILE CANCER (Ca Penis)

- Jackson's grading/staging is used for classification.
- Premalignant conditions predisposing to Ca penis are
 - Erythroplasia of Queyart,
 - Bowen d/s
 - Papillomatosis
- Other risk factors:
 - HPV types 16 and 18 (Basaloid and warty verrucous varieties in more than 90% of cases)

- Phimosis and chronic irritation
- Gonorrhea, HPV
- Smoking
- Neonatal circumcision gives protection against the disease..
- The best prognostic factors related to survival are the presence of positive **lymph nodes**, the number and site of positive nodes and the extracapsular nodal involvement.
- Predictive factors for the presence of lymph node metastasis
 - location, size, tumour grade, corpora cavernosa invasion etc.

GYNAECOLOGICAL CANCERS

ENDOMETRIAL CANCER

- M/c gynaecological malignancy worldwide.
- Peak incidence 55-69 years (d/s of postmenopausal women).
- **Risk factors**
 1. Endometrial hyperplasia d/to exposure to unopposed estrogen stimulation from either endogenous (**PCOD, DUB, fibroid**), **functional ovarian tumour** or exogenous sources (ERT in post-menopausal women).
 2. Familial predisposition
 3. Obesity, HTN, DM, Low fertility index (infertile women with fewer children)
 4. Early menarche / late menopause, postmenopausal bleeding, altered menses
 5. Premenopausal women with prolonged anovulation.
 6. Women taking Tamoxifen for breast cancer and exogenous estrogen (HRT with estrogen)
 7. Nulliparity
 8. H/o previous breast cancer
 9. **Corpus cancer syndrome** comprise of DM + HTN + obesity. It is seen in family with DM, hypertension, and taking fat rich diet.
 10. HNPCC
- **Risk of progression to malignancy**
Maximum risk is a/w cellular atypia & complex hyperplasia

- Simple hyperplasia without atypia	→ 1%
- Simple hyperplasia + atypia	→ 8%
- Complex hyperplasia without atypia	→ 3%
- Complex hyperplasia + atypia	→ 29%
- OCPs & smoking also have some protective effect.
- **Clinical features**
Abnormal vaginal discharge (90%), postmenopausal bleeding / menometrorrhagia (80%), leukorrhea (10%)
- **Diagnosis**
 1. Endometrial biopsy will almost always detect an endometrial ca with cytological sampling
 2. Curettage first of endocervix then of the endometrial cavity, with careful examination under anaesthesia is considered the most definitive method of diagnosing and clinically staging the disease
 3. Myometrial involvement is suspected if the corpus is enlarged for which MRI is helpful.
- *Cervical pap smear is not effective in detecting endometrial cancer*
- *Adenocarcinoma is m/c histological variety (75-80%), most differentiated form adeno-acanthoma is seen in 10% and poorly differentiated form is adenosquamous Ca*
- *Women with suspicious or abnormal pap smears should have colposcopic directed cervical biopsies*
- *Colposcopic directed biopsy is required when any lesion is visible on the cervix, regardless of pap smear findings. But cone biopsy is still required when endocervical tumour is suspected*
- **Staging**
Requires surgery
- **Metastasis**
 1. Occurs to vagina, regional pelvic /para-aortic LN, ovaries, lungs, brain and bone
 2. The most frequent site of recurrence following treatment for endometrial Ca is **vaginal vault**
- **Prevention**
Progesterone therapy in anovulatory patient and in postmenopausal women (receiving estrogen replacement) will ↓ the risk of development of endometrial cancer
- **T/t** : Total AH + B/L salpingo-oophorectomy (Pan hysterectomy) is the definitive t/t for endometrial cancer

Remember

- *If the pelvic LN are involved, then it is stage III in the endometrial cancer but stage IV of Ca cervix*

RISK FACTORS & T/T of Ca ovary, Ca Endometrium & Ca Cervix

	Ca Ovary	Ca endometrium	Ca Cervix
<i>Risk factors</i>			
1. Mean age group	> 60	55-65	45-55
2. Mechanism	Disordered ovarian function	Unopposed estrogen stimulation	Early onset of sexual activity Frequent miscarriages
3. Menstrual relation	Early menarche / late menopause (↑ no. of ovulation years)	Early menarche / late menopause	
4. Parity	Nulliparity	Nulliparity	Multiparity
5. Fertility Index, sexual pattern	Low (Infertility)	Low (Infertility)	Multiple sexual partners High risk male partner
6. Socio-economic status (SES)	-	High	Low SES
7. Associations	Turner's syndrome	Obesity, HTN, DM	Smoking, organ transplant
6. Personal Hx/ association	H/o breast & endometrial cancer	H/o breast Ca	STD, HIV, preinvasive lesions, Viruses HPV 16, 18, 31; HSV2, HPV type 16 is m/c → SqCC HPV type 18 → Adenoca
7. Family Hx	First degree relatives with h/o ovarian cancer (mother/sister)	Endometrial Ca, breast Ca (1st degree relatives)	
8. Drugs	Clomiphene (ovulation induction)	Tamoxifen, HRT with estrogen	OCPs, POPs, alcoholism, drug abuse, immunosuppression
<i>Risk decreases with</i>	Risk ↓es with each pregnancy (↓ by 10%), breast feeding, tubal ligation	Progestins added to HRT ↓ risk Use of OCPs have protective effect	
<i>T/t</i>	<p>Stage Ia & Ib, grade I</p> <p>Premenopausal --- staging laparotomy then u/l oophorectomy</p> <p>Stage Ia/b (grade 2/3), Ic, IIa, IIb (resectable)</p> <p>TAH/BSO → Staging → Adjuvant Rx (Taxol + Carboplatin or CAP or C+P) or Radiotherapy.</p> <p>Radical trachelectomy upto IIA</p> <p>Stage IIb (irresectable), IIc, III & IV</p> <p>Cytoreductive Sx → Adjuvant Chemo for 6 cycles if microscopic d/s + nt</p>	<p>Stage 0 TAH/BSO</p> <p>Stage I Pan hysterectomy</p> <p>Stage II</p> <p>TAH/BSO → Post op radiotherapy</p> <p>Stage III</p> <p>TAH/BSO → LN sampling + Post op radiotherapy</p> <p>Whole body radiation is reqd in stage IIIC & IV</p>	<p>Stage Ia₁ Hysterectomy</p> <p>Stage Ia₂, Ib, IIa, Radical Hysterectomy + b/L LND or Ext. Radiotherapy + ICRT (Brachy)</p> <p>IIb</p> <p>Preop radiotherapy → Sx → Post op radiotherapy or only radiotherapy</p> <p>Stage III & IV</p> <p>Radiotherapy</p>

STAGING of Ca ovary, Ca Endometrium & Ca Cervix

Stage	Cervix	Endometrium	Ovary
0	In situ	In situ	
IA	Horizontal spread ≤ 7 mm invasive cancer diagnosed only by microscopy, stromal invasion ≤ 3 mm (IA ₁) 3-5mm (IA ₂)	Limited to endometrium	Limited to <i>one ovary</i> , no tumour on external surface, PC -ve, capsule intact
IB	Macroscopically visible lesion / with spread > 7 mm, size ≤ 4 cm (IB ₁) and > 4 cm (IB ₂)	Invasion $< \frac{1}{2}$ of myometrium	like IA but <i>both ovaries involved</i>
IC	-	Invasion $\geq \frac{1}{2}$ of myometrium	IA or IB + surface tumour ⁺ + PC +ve / ascites +nt, capsule ruptured
IIA	Invasion b/w uterus & pelvic wall Lower 1/3 rd vagina without parametrial involvement	Endocervical gland involved only	Tumour extending to pelvis, metastasis to uterus / tubes
IIB	above + parametrium involvement	Cervical stromal invasion	Other pelvic tissue
IIC	-	-	IIA or IIB with surface ⁺ , PC +ve/ capsule ruptured, ascites +
IIIA	Involves lower 1/3 rd of vagina but $<$ pelvic wall	Invasion of serosa / adnexa / peritoneal metastasis (+ve cytology)	Tumour extent $>$ pelvis /LN/SI/ omentum / liver surface Microscopic disease of A/P surface, LN -ve
IIIB	\geq pelvic wall or causes hydronephrosis / non-functioning kidney	Vaginal metastases	A/P surface implant < 2 cm, LN -ve
IIIC	—	Metastasis to pelvis/paraortic LN	A/P surface IIIB but > 2 cm / LN +ve
IVA	Invasion of bladder/bowel/mucosa	Invasion of bladder/bowel mucosa	Distant metastasis to liver parenchyma/ pleural effusion (stage 4)
IVB	Distant	Distant metastases (lung/brain/bone)	

[A = Abdominal, P= Peritoneal, PC = Peritoneal cytology]

CERVICAL CANCER (Ca-Cervix)

- Bleeding PV is the **m/c** symptom. It is in the form of irregular menses, post coital bleeding. Discharge is offensive.
- Deep pelvic pain, backache, urinary incontinence.
- **M/c** site of starting point : **Squamocolumnar junction** in ectocervix
- Best method of screening : Pap smear
- Inv used in FIGO staging : FDG - PET is gold standard.
- Best method of confirming d/g : Cx biopsy.
- Conservative surgery (surgery to retain conception/childbearing function) is done in young women with early stages. **Trachelectomy**, also cervicectomy, is a surgical removal of the uterine cervix

OVARIAN CANCER

- Drugs used in chemotherapy : Combination of carboplatin + paclitaxel.
- **Details in gynae section.**

Ca-FALLOPIAN TUBE

- Benign tumours of FT are rare and primary carcinoma is the **m/c** malignant lesion
- Women with BRCA1/2 mutations are at risk of Ca-FT.
- **Postmenopausal bleeding** is the usual presenting symptom. There may be h/o intermittent profuse discharge (*hydrops tubae parovialis*)

- Usually adenocarcinoma
- TOC: Pan-hysterectomy (TAH + B/L salpingo-oophorectomy)

Ca-VULVA

- Mainly Sq CC
- HPV plays a role in etiology
- Vulvar intraepithelial neoplasia is common in premenopausal women and is pre-cancerous condition
- M/c site : labium majus
- Cl/f. lesions are usually multiple (2/3rd)
- There may be submucosal spread of the tumour cephalad to involve the vagina and urethra (**urethral metastasis**) or there may be involvement of the post vulvar with invasion of the anus/rectum
- T/t
 - Vulvar intraepithelial neoplasia: localised wide excision / laser
 - Multifocal / diffuse: skinning vulvectomy with split thickness graft
 - Microinvasive lesion (<1 mm invasion): wide local excision with 1 cm margin
 - Other lesion – Radical local excision + 2 cm margin + LN dissection

BONE TUMOUR

Metastatic Bone Tumours

- Commonest form of cancer affecting skeleton is metastatic tumour deposits (secondaries) from primary lesions elsewhere in the body. 80% of these metastatic lesions are from primary cancers, particularly of **breast** > prostate > lung > kidney > thyroid > pancreas > stomach in that order of frequency.
 - M/c symptom of metastatic bone tumours – pain
 - Radiological finding: usually osteolytic lesions, but in case of breast metastasis is either partly or solely osteoblastic.
- Prostate secondaries are purely osteoblastic**

→ Bone tumour which is hormone dependent ---fibrous dysplasia

→ M/c malignancy of bone: secondaries (metastatic breast cancer)

→ M/c primary malignant bone tumours in descending order of frequency

MM > osteosarcoma > chondrosarcoma > Ewing's > GCT

→ M/c primary bone tumour located in vertebra. Giant osteoid osteoma (osteoblastoma)

Matrix forming bone tumors

Are 2 types :

1. Chondrogenic / cartilage forming

Osteochondroma, chondroma, chondroblastoma, chondromyxoid fibroma, chest wall hamartoma, chondrosarcoma

2. Osteogenic/bone forming

Osteoid osteoma, osteoma, osteosarcoma

EWING'S SARCOMA (Ewing's tumour)

- 'Primitive neuroectodermal tumour' (PNET).
- **Small blue round cells** are seen. Also included in the category of small blue round cell tumour.
- Occurs in 2nd decade during the period of rapid growth. (Remember : M/c bone tumour of first decade is also Ewing's sarcoma)
- **Small blue round cells** are seen
- It is seen in flat bones of pelvis and diaphysis of femur & tibia (diaphysis- metaphysis location)
- t(11:22) is found in 80-95% of cases, which gives definitive clue in d/g.

Presence of p30/32 a product of mic2 gene is the cellular marker for Ewing's sarcoma.
- X-ray: "onion skin appearance" with lytic and concentric multilaminar periosteal reaction
- T/t: Radiation + CT combined therapy followed by anatomically feasible resection or wide excision
- Locally malignant
- Fever, anemia, male sex, high LDH and leucocytosis are a/w poor prognosis. fever may be the first sign of recurrence.
- Most important prognostic factor is presence of detectable metastasis at the time of presentation.

OSTEOSARCOMA

- M/c primary malignant tumour of bone
- M/c in age group – 10-25. Common in adolescent males
- Commonest site: metaphysis of long bones (lower end of femur > upper end of tibia > proximal humeral metaphysis > pelvis > proximal femur)
- **Risk factors**
 - Radiation (commonest)
 - Paget's disease
 - Inactivation of Rb suppression gene
- Lymphatic involvement is not common

- It occurs in spindle cells that produce osteoid
- It presents with local pain and swelling often noted after trauma
- X-ray: "sunburst appearance" or sunburst appearance d/to new bone formation with sclerotic > lytic lesion. Codman's triangle are d/to periosteal elevation.
- Early metastasis to lung > bone (**Bone tumour with calcified secondaries**).
- TOC: Ablative surgery (usually amputation) and chemotherapy. O~ is radioresistant
- Myositis ossificans must be distinguished from extraskeletal osteosarcoma (mimics histologically)*
- Secondary osteosarcoma**
O~ in older age group (>40 yr) secondary to Paget's disease, irradiation, multiple hereditary exostosis, polyostotic fibrous dysplasia, multiple osteochondromas, diaphyseal aclasis, survivors of RB, bone infarcts.
- Histological feature of osteosarcoma**
 - "Neoplastic new bone formation in sarcomatous stroma" is the most characteristic
 - Highly malignant, pleomorphic, spindle cell neoplasm
 - Malignant cells form osteoid or bone.

Histological /Radiological features of some bone tumours: extract

Tumour	Characteristic histology
Osteosarcoma	Neoplastic new bone / osteoid formation in sarcomatous stroma is hallmark. Bone tumour with calcified (sclerotic) secondaries.
Ewing's sarcoma	Small, blue round cells with PAS +ve diastase, bone destruction
Osteoid osteoma	Lucent nidus of osteoblastic tissue surrounded by reactive sclerosis
Chondrosarcoma	Bone tumour with dense calcification.
Chondroblastoma	"Chicken wire" calcification
Osteoclastoma (GCT)	Multinucleate giant cells in large number (>15 nuclei/cell)

Radiological appearance of bone tumours

- Sunburst appearance → Osteosarcoma
- Onion peel appearance → Ewing's sarcoma
- Driven screw appearance → Pindborg's tumour
- Trethowan's sign → SCFE
- Spiculated/ mottled/patchy calcification → Chondrosarcoma
- Honey comb appearance → Adenoma

- Aneurysmal sign → TB spine
- Wormian bones → Osteogenesis imperfecta
- Fallen fragment sign → Simple bone cyst

OSTEOCLASTOMA /GCT (giant cell tumour)

- Female predominant tumour (F:M ratio 3:2)
- Sites : distal femur/proximal tibia, lower end radius, proximal humerus.
- It is almost never seen before closure of epiphyseal plate, age group 20-40 years. It arises from epiphysis.
M/c location is subarticular
- Chief symptom: pain
- CV sign: egg shell cracking on palpation
- X-ray: Cystic expansile lesion with "Soap bubble appearance". little reactive bone at the margins
- 98% cases are benign with potential for metastasis. Benign GCT may recur and may become malignant.
- Neoplastic portion is the mesenchymal stromal cells rather than the giant cell element
- T/t: Thorough curettage and grafting is standard initial treatment depending upon site.
Lower end of ulna, upper end of fibula---excision
Lower end of radius---Local resection (excision) with fibular grafting
Lower end of femur, upper end of tibia---excision with turn-o-plasty
Vertebral---Radiation
If tumour recurs---biopsy and look for malignant change - if not, resection followed by allograft.

Chondrosarcoma

- M/c malignant cartilaginous tumour
- Most often located in pelvis and upper end of femur
- Risk factors-Multiple osteochondromas, Ollier's disease, age >30 yr

Benign Bone Tumours

Osteoid osteoma

- M/c true benign bone tumor
- Sclerotic lesion in the cortex of femur diaphysis. It has radiolucent nidus surrounded by dense sclerotic bone
- Produces nocturnal pain relieved by NSAIDs (Aspirin)

Chordoma

- Locally malignant tumour with bad prognosis
- M/c site: Sacrococcygeal region of spine (other sites are clivus, vertebral body)

- Arises from remnant of notochord
- Histo: physaliform cells
- Chondroid chordoma is a variety which occurs at base of skull & has good prognosis

Osteochondroma (Bony exostoses)

- M/c bone tumour. Comprise 45% of benign bone tumours (not true bone tumour)
- <20 yrs
- Metaphysis/diaphysis
- Distal femur, proximal tibia, and proximal humerus are M/c sites.
- Very slow growing tumours
- X-ray: Sessile/pedunculated bony stalk with **cartilaginous cap** extending from the metaphyseal region near the epiphyseal plate.
- Cortex & cancellous bone of osteochondroma blends with the cortex and cancellous bone of host.
- Causes of sudden increase in pain---Sarcomatous degeneraⁿ. fracture, bursitis

Enchondroma (Chondroma)

- Mean age – mid thirties
- Occurs m/c in **hands**, including metacarpals and phalanges (followed by proximal end of humerus)
- X-ray – cystic expansile lesion in the shaft(diaphysis of a long bone), *speckled calcification*
- T/t – curettage + grafting by bone chips.

- Multiple congenital osteochondromas are also k/as exostoses & have AD inheritance, growth retardation and bowing deformity of the long bones.
- Most common lesion / tumour of hand is – enchondroma
- Other bone tumours with calcification is chondroblastoma (mottled or chickenwire calcification)
- Maffucci syndrome: hereditary multiple enchondroma + cavernous hemangioma
- Ollier's disease: non-hereditary disease of childhood, multiple non-ossifying enchondromas arising from medullary cavity of bones
- Chondrosarcoma is characterized by--- Expansile lesion with endosteal scalloping & punctate calcification

Simple (Solitary) or Unicameral bone cyst

- Centric expansile radiolucent lesion
- <20 yr of age, M>F
- **Metaphyseal**
- Site: Upper end/proximal humerus (50%), proximal

femur(25%)

- Cl/f: Usually asymptomatic/ pain in shoulder
- X-ray: Multilocular, central, cystic expansile & lytic lesion radiolucent lesion. **Fallen fragment sign** (fractured cortex settles in the most dependent portion).
- Gross: Cyst is fluid-filled (serous or sero-sanguineous) space with a thin capsule/ shaggy fibrous layer
- C/c: pathological #
- T/t: Subtotal resection, with excision of most of the cyst including bone shell

Aneurysmal bone cysts

- Eccentric metaphyseal lesion
- <20 yrs, 2nd decade (M:F = 1:1)
- M/c in metaphyses of long bones (upper tibia) and vertebrae especially post. elements
- X-ray app: eccentric blowout/ ballooned out radiolucent lesion, expansile cysts and septa, locally destructive by expansile growth (lytic lesion) but do not metastasize
- Gross: tumour is blood-filled cavity. Contain numerous multinucleate (nuclei <15/cell) giant cells.
- Trabeculated/bubbly appearance d/to pseudoloculations.
- T/t: Curettage and bone chip grafting

Pott's puffy tumour: It is not a tumour. It is osteomyelitis of the frontal bone with cellulitis of the frontal region of the scalp. It may spread intracranially through emissary vein which endangers the life of the patient.

Eosinophilic granuloma

- Solitary lytic lesion of the bone
- M/c site is skull
- Peak incidence b/w 7-8 years male
- Pain is the presenting symptom
- X-ray: **lytic** defect within long bones frequently expands the shaft, *periosteal new bone formation* also seen
- T/t - usually self limited. Tendency of healing following biopsy with or without grafting
 - low dose radiation

Admantinoma

- Also k/as **ameloblastoma/ adamantine epithelioma**
- M/c site is posterior mandible in molar teeth area (Tibial diaphysis is another site)
- Benign but locally invasive, slow growing cystic tumour with 'egg shell crackling' on palpation.
- TOC ---Wide resection

Location of Bone Tumours

- Diaphysis in → Ewing's tumour, Enchondroma
 Metaphysis in → Osteochondroma, Osteosarcoma
 Epiphysis in → Chondroblastoma/Codman's tumour
 Giant cell tumour

[Mnemonic is Demo ECG --- DEE MOO ECG]

- M/c bone tumour in epiphyseal region before epiphyseal fusion is → chondroblastoma and after epiphyseal fusion is osteosarcoma
- GCT arises from metaphysis and extends into epiphysis [So, only if Mc site / location is asked then only epiphysis will be the answer]
- Common Malignancies in Bone - Secondaries (m/c) > multiple Myeloma > osteosarcoma
- Multiple myeloma is commonest primary malignancy of bone.
- Osteosarcoma is the m/c primary malignant-tumour of long bones.
- Osteoid Osteoma is m/c true benign tumour of bone (Osteochondroma is m/c benign tumour but not true neoplasm of bone)
- Secondaries in bone comes from (KPT BB) 60% from breast and prostate, bronchus, kidney, Thyroid
- Metaphyseal translucencies are the earliest and characteristic feature of childhood leukemia.

SOFT TISSUE SARCOMAS

C/T	In Children	In Adults
M/c type	Rhabdomyosarcoma	Malignant fibrous histiocytoma
M/c site	Head & neck	LL, esp thigh
T/t	WLE	WLE

- Occurs in elderly. Size usually >5 cm
- Classically, soft tissue sarcoma present as asymptomatic large masses in the extremities or retroperitoneum, but may also develop in neck and abdomen viscerae. Most sarcomas arise de novo
- Origin: from mesenchymal cells and include liposarcoma, fibrosarcoma, rhabdomyosarcoma, leiomyosarcoma and desmoid tumours
- Hematogenous spread (to lungs) is common.
- Both CT and MRI are useful MRI is the best
- Prognosis depends upon size and grade
- T/t: Staging followed by **surgery (wide local excision)**

- Most likely cause of a firm 9 cm mass in mid-thigh of a 63 yr old man → malignant fibrous histiocytoma
- Intraoperative radiation therapy to the tumour bed may be useful in case of retroperitoneal and abdominal soft tissue sarcoma.
- M/c retroperitoneal tumour → Liposarcoma

Desmoid tumour

- Low grade soft tissue sarcoma that do not metastasize.
- Musculoaponeurotic fibromatosis
- Often occur in abdominal wall scars or after parturition in females in patients with Gardner's syndrome.
- T/t is wide excision.
- Local recurrence occurs in 1/3rd cases. Adjuvant radiation therapy produces reduced incidence of recurrence.

Lymphangiosarcoma

Chronic extremity lymphedema and tissue irradiation increases the risk for lymphangiosarcoma. A classic example is the development of upper extremity lymphangiosarcoma in patients with a postmastectomy lymphadenomatous arm.

Synovial sarcoma

- Malignant soft tissue tumour which arise from primitive synovium like cells.
- Occurs in young adults 15-35 age group.
- Usually extra articular and affects lower limb. Among joints knee is m/c site.
- SYT-SSX fusion gene determines morphology & prognosis in synovial cell sarcoma.

M/C SITES OF METASTASIS

Commonest metastatic sites in descending order

- Breast ---- Lung > bone > liver > adrenal > brain
- Colorectal Ca ---- Liver > Adrenal > bone > lung
- Lung Ca ---- Liver > bone > Adrenal > brain
- Prostate Ca ---- Bone > lung > liver
- Site of metastasis for carcinomas --- Regional lymphnode.
- Site of metastasis for sarcomas --- Lungs through blood stream
- Most common site of metastasis overall --- LN > liver.

PARANEOPLASTIC SYNDROMES & CANCERS

- Hypoglycemia -- Hepatoma (HCC) & mesothelioma
- Hypercalcemia -- SqCC of lung, multiple myeloma, Metastasis from breast Ca, RCC
- Secondary polycythemia (Erythropoietin production) -- Renal adeno Ca. (hypernephroma) & Wilm's tumour
Hepato cellular Ca.
Hemangioblastoma cerebellar (V.H.L. syndrome)
Hydronephrosis (Remember '5' H)
- SIADH -- Oat cell/SCLC, brain tumours
- Cushing syndrome -- SCLC
- Polymyositis, dermatomyositis and cerebellar degeneration -- SCLC

- Hypo gammaglobulinemia is seen with --- CLL, Multiple myeloma, thymoma
- Pulmonary osteoarthropathy (HPOA) & Clubbing is seen in --- Primary lung ca.
- Superficial migratory thrombophlebitis is seen in --- Pancreatic ca., stomach ca.
- DIC is seen in --- M_3 AML (promyelocytic AML), Mucinous adenocarcinoma (ca pancreas, lung, prostate)

SOME POINTS OF SPECIAL MENTION

- All carcinoma / malignant tumours metastasize except --- Glioma & BCC
- Benign tumour that metastasize --- Invasive mole.
- Site of metastasis for carcinomas --- Regional lymph node.
Site of metastasis for sarcomas --- Lungs
- Usually benign tumours are capsulated except --- Hemangioma (locally malignant), Leiomyoma of uterus, Dermatofibroma
- Usually malignant tumours are not capsulated except --- Follicular ca. thyroid, RCC [Malignant but capsulated]
- Usually benign tumours do not turn into malignant except multiple adenomas of large intestine --- Adeno Ca.
- Neurofibromatosis may develop into --- Sarcoma

- Malignant neoplasms which are well differentiated --- SqCC of epidermis, adeno carcinoma thyroid, HCC
- Growth factors affecting degree of differentiation of malignant tumours: - EGF, FGF, CSF, PDGF, TGF- β , IL
- Carcinomas usually metastasize by lymphatic route. Carcinomas that invade blood vessels are
 - Renal adenocarcinoma (most common)
 - Follicular cell Ca of thyroid
 - HCC
- Sarcomas usually metastasize by hematogenous route exception is
 - Rhabdomyosarcomas (m/c sarcoma that invade lymphatics)
- Example of tumours whose metastatic potential is based on size :-
 - Renal adenocarcinoma (>3 cm malignant, <2 cm benign)
 - Carcinoid tumours (>2cm can metastasize, <2cm do not)
- Retrograde metastasis seen in (d/t obstruction of lymphatic by tumour cell)
 - Krukenberg tumour
 - Metastasis of Ca-prostate to supraclavicular LN
 - Metastatic deposit in adrenals from Ca-Lung
- Skip metastasis is seen in bronchogenic Ca
- Lung to lung metastasis (transbronchial spread) is seen in bronchoalveolar ca. of lung.

SOME IMP. NEGATIVE POINTS

- Radiation can cause all leukemias except CLL.
- Hypercalcemia is NOT seen with --- Basal cell Ca
- Serum levels of angiotensin converting enzyme (ACE) are NOT elevated in --- bronchogenic carcinoma
- Hormone NOT produced by small cell lung carcinoma --- PTH
- Investigation not required in diagnosis of osteosarcoma --- B M biopsy
- NOT a benign bone tumour --- Chordoma, MM, Chondromyxoid fibroma, Osteochondroma, Chondroblastoma
- Chordoma is NOT seen in --- Ribs
- Tumour NOT seen in childhood --- Plasmacytoma
- Thymoma is usually NOT a/w --- SIADH

- Psammoma bodies are NOT seen in ---- Follicular and medullary carcinoma of thyroid
- Does NOT occur in RCC --- Malignant hypertension
- Smoking is NOT a/w --- Nasopharyngeal carcinoma, cancers of liver, endometrial cancer
- NOT true of carcinoids --- Rectum is a rare site
- NOT true of FAP --- Autosomal recessive
- Hilar lymphadenopathy and cavitation are NOT seen in --- Oat cell cancer of lung
- NOT recommended in screening of prostate cancer --- TRUS
- NOT a risk factor for Ca endometrium --- smoking, OCP use
- NOT a premalignant GI polyp --- Juvenile polyp
- NOT true about p53 --- Wild p53 non mutated gene is a/w childhood neoplasms.
- NOT a tumour suppressor gene --- k-RAS
- Colon carcinogenesis is NOT a/w --- B-Catenin
- Kaposi sarcoma is NOT a/w --- HBV
- Rituximab --- is NOT used in PNH
- Infliximab --- is NOT used in SLE

CLINICAL VIGNETTE

- A 25 year old lady present with nipple discharge from the left breast. On examination the discharge is bloody and is localized to one duct. Ultrasound is suggestive of a dilated duct with an intra-ductal mass. The most appropriate surgical procedure for her would be:

- A. Radical duct excision
- B. Partial Mastectomy
- C. Microdochectomy.
- D. Modified radical mastectomy

(Ans. C. Microdochectomy)

Lady in the qn is most likely suffering from duct papilloma which is treated by Microdochectomy

- A 40 years old female patient presented with recurrent headaches, MRI showed an extra-axial, dural based and enhancing lesion. The most likely diagnosis is:

- A. Meningioma. B. Glioma.
- C. Schwannoma. D. Pituitary adenoma.

(Ans: A. Meningioma)

In meningiomas the radiologic image of a dural based extra-axial mass with dense, uniform contrast enhancement is essentially diagnostic.

- A 9 yr old child is operated for papillary carcinoma of thyroid with near total thyroidectomy and neck dissection. Which of the following would be next best step of management?

[AIPGMEE 2012]

- (A) TSH suppression
- (B) Follow-up with Whole body I-131 nuclear scan for metastases
- (C) Postoperative local external beam radiation to prevent recurrence
- (D) CECT neck to look for residual / recurrent cancer

(Ans: A. TSH suppression)

- A 37 year old lady has been diagnosed to have left breast cancer with axillary lymph node metastasis. She has undergone modified radical mastectomy. Her post-operative treatment should include:

- A. Adriamycin based chemotherapy
- B. Chemotherapy followed by Tamoxifen if estrogen/progesterone receptors are positive.
- C. Concurrent adriamycin based chemotherapy + Tamoxifen.
- D. Chemotherapy is not indicated.

[AIPGMEE 2008]

(Ans: Chemotherapy followed by Tamoxifen if estrogen/progesterone receptors are positive)

- A 65 year old miner has lost 7 kgs weight within two months, has presented with cough, and blood streaked sputum. He was treated for pulmonary tuberculosis 10 years ago. He also has dropping of his left eyelid for one month. On physical examination, there is ptosis of the left eye and papillary miosis. Chest X-ray revealed round opacification in the left upper lobe. What is the most probable diagnosis? [AIIMS May'06]

- A. Secondary tuberculosis.
- B. Adenocarcinoma.
- C. Squamous cell carcinoma.
- D. Asbestosis.

(Ans: C. Squamous cell carcinoma)

Cough, hemoptysis and loss of weight in an elderly arouse the suspicion of malignancy. Points in support are Drooping of eyelid + ptosis + miosis are s/o Horner's syndrome which is commonly a/w Pancoast tumour.

Histologically it is a SqCC and m/c involves apical lobe of lung. Pulmonary TB in past is considered a risk factor for dypt of SqCC

- A 15-year-old boy is injured while playing cricket X-rays of the leg rule out a possible fracture. The radiologist reports the boy has evidence of an aggressive bone tumor with both bone destruction and soft tissue mass. The bone biopsy reveals a bone cancer with neural differentiation. Which of the following is the most likely diagnosis?

[AIIMS May'06]

- A. Chondroblastoma.
- B. Ewing's sarcoma.
- C. Neuroblastoma.
- D. Osteosarcoma.

(Ans. B. Ewing's sarcoma)

"Bone cancer with neural differentiation" is the clue. As it may be either neuroblastoma or Ewing's sarcoma, but the age group, site and aggressiveness favours Ewing Sarcoma.

- A 67 male presented with cough and haemoptysis. Bronchoscopic biopsy showed undifferentiated tumor cells. Which immunohistochemical maker will be useful in diagnosis?

[AIIMS Nov'09]

- A. Cytokeratin
- B. Vimentin
- C. Calretinin
- D. Desmin

(Ans. Cytokeratin)

SqCC is the m/c lung carcinoma seen in elderly and chronic smoker. Histologically SqCC arise from lung epithelium. Cytokeratin is a marker for epithelial tumours or carcinoma.

- A 60 year old chronic smoker male presented with a h/o gross total painless hematuria of 1 day duration. Investigation of choice is:-

[AIIMS May '10]

- A. Urine for malignant cytology
- B. USG abdomen
- C. Blood culture
- D. CT KUB region

(Ans. A. Urine for malignant cytology)

Bladder cancer is the m/c cause of sudden onset gross total painless hematuria in elderly. Malignant cells are +ve in urine.

- A 40 year old male presents with bouts of hematemesis. Endoscopic biopsy revealed GIST. USG rules out dissemination. The case is proceeded with laparotomy. On opening the abdomen the surgeon sees the tumour at the

joint of body and antrum infiltrating into the tail of pancreas. Next step in management of this patient is:

[AIPGMEE '10]

- A. Close the abdomen
 - B. Distal antrectomy alone
 - C. Pyloroplasty
 - D. Distal antrectomy with splenectomy and pancreatic tail resection
- (Ans. D. Distal antrectomy with splenectomy and pancreatic tail resection)

GIST (GastroIntestinal Stromal Tumours)

- Slow growing submucosal tumours
- Originates from **interstitial cells of Cajal**, which control intestinal peristalsis
- 66% are located in **stomach** (m/c site)
- 85% of GISTs have **c-KIT** mutations.
- 95% of them stain with anti c-KIT antibodies (**CD117**)
- **Carney's triad** is :
Gastric GIST + Paraganglionoma + pulmonary chondroma
- D/g is made by endoscopic biopsy.
- Metastasis occurs by hematogenous route.
- Surgery is the t/t of choice
 - If GIST is localised --- Resect the tumour f/b C-kit antigen (CD 117). Wedge resection with clear margins is adequate, If safe, en bloc resection of surrounding structures c/b considered
 - If GIST is localised but unresectable --- Imatinib
 - If Recurrent or metastatic d/s --- Resect the primary with minimal metastatic d/s f/b Imatinib.
- PET is useful in predicting response to therapy.

- A 35 year old 3 +0 female presents with post coital bleed. On colposcopic examination one quadrant shows CIN grade III. Next step in management of this patient is:

[AIIMS May '10]

- A. Cryotherapy
 - B. LEEP
 - C. Conisation
 - D. Hysterectomy
- (Ans. C. Conisation)

Cervical conisation removes ectocervical lesion and a portion of endocervix by means of a cone shaped tissue biopsy. It is a safe, effective means to treat CIN, CIS (Cervical carcinoma in situ), and AIS (adenocarcinoma in situ).

Current t/t of CIN is limited to local ablation or excision procedures. Laser or LEEP conisation are alternative methods.

NOTES

- A 35 year old P3 +0 has undergone radical hysterectomy with biopsy shows stage IB cancer cervix with involvement of outer 1/3rd of cervix and lower uterine segment involvement. Next step in management of this patient is:

[AIIMS May '10]

- A. Chemotherapy
- B. Chemoradiation
- C. Radiation
- D. Follow up

(Ans. D. Follow up)

Patient has Ca cervix stage IB₁ as per FIGO staging. FIGO IB₁ includes clinical lesion < 4 cm in size. Wertheim hysterectomy is the TOC upto stage IIA Hysterectomy has already been done so follow up is required see metastatic spread and t/t plan.

- A 24 year old male presented with retroperitoneal and necrotic mass near the hilum of left kidney which showed heterogenous contrast enhancement on CECT. Most probable diagnosis is:

[AIIMS May '10]

- A. Metastatic transitional cell carcinoma
- B. Metastatic melanoma
- C. Metastatic germ cell tumour
- D. Lymphoma

(Ans. C. Metastatic germ cell tumour)

Retroperitoneal necrotic mass near the hilum most likely represent lymph nodes. Testicular malignancy commonly spreads to retroperitoneal lymph nodes near renal hilum. In lymphoma necrosis is very rare before radiation. Testicular germ cell tumours generally metastasize in the region of renal hilum, lymph nodes show high intensity signals on T2 weighted images on MRI.

INTERPRETATION OF A HEMOGRAM

- RDW is useful in differentiating IDA from thalassemia.
- Left shift index :
Left shift is seen in → Neutrophilia & infections
Right shift is seen in → Anemia & pregnancy
- Crook Armeth counts : Counts of lobes in neutrophils

Characteristic hematological changes

Leukocytopenia	- Typhoid - Rickettsial infection
Monocytosis	- Brucellosis - Lymphoma - Typhoid, TB
Lymphocytosis	- Mumps - IM - Pertussis
Coomb's negative	- HS, HUS - Wilson's d/s - TTP
↓LAP-Score	- CML - PNH
↑ LAP-Score	- Aplastic anemia, Pernicious anemia - Leukemoid reaction - Polycythemia vera, - Steroid t/t - Myeloid metaplasia (may be normal or ↓)
Plasmacytosis in bone Marrow (↑ number of plasma cells)	- MM - Aplastic anemia - RA, SLE, liver cirrhosis - Metastatic Ca., chronic inflammation
Hypergammaglobulinemia	- HIV - Sarcoidosis - Kala-azar - Sickle cell anemia

- Pancytopenia with hypocellular and fatty marrow is seen in --- Fanconi anemia
- Pancytopenia with plasmacytosis in marrow is seen in --- Aplastic anemia

Important cells in PBS

Cell type	Found in cells	Clinical conditions
Spherocytes	RBCs	HS, AIHA, ABO-HDN, G-6-PH def., hypersplenism
Target cells	RBCs	Thalassemia, HbS, Hb-C, liver disease
Schistocytes (fragmented RBCs)	RBCs	Thalassemia, iron deficiency, megaloblastic anaemia, microangiopathic AIHA, severe burn
Burr cells / helmet cells	RBCs	Uraemia, HUS
Tear drop RBCs	RBCs	Myelofibrosis
Heinz bodies	RBCs	G6PD deficiency
Howell-Jolly bodies	In circulating RBCs	After splenectomy, megaloblastic anemia, severe hemolytic anemia
Dohle bodies	Neutrophils	Burns, infections
Punctate basophilia	RBCs	Lead poisoning, aplastic anaemia, thalassemia, myelodysplasia

- Ring sideroblasts are seen in--- Sideroblastic anemia, Myelodysplastic syndrome.

MICROCYTIC HYPOCHROMIC ANEMIA

Iron Deficiency Anemia (IDA)

- IDA is the m/c cause of anemia worldwide and in India. It is the commonest nutritional deficiency disorder

Clinical and genetic classification of thalassemia

Clinical class	Genotype	Molecular Defect	Hb level	Disease	Hb electrophoresis
β-thalassemias					
1. Major	homozygous β^0/β^0 Homozygous β^+ β^+/ β^+		< 5 gm%	Severe congenital hemolytic anemia required BT	HbA 0% HbF 50-96% HbA ₁ 4-10%
2. Intermedia	β^0/β^0 β^+/ β^+		5-10 gm%	Severe but do not require regular BT	Variable HbA 0-10% HbA ₂ 4-10% HbF 90-96%
3. Minor (carrier)	β^0/β or	β^+/ β	10-12 gm%	Asymptomatic	HbA ₂ (4-9%) HbF 1-5%
α-Thalassemias					
1. Hydrops fetalis	-/- -/-	Deletion of all four α -genes	3-10 gm%	Fatal in utero or in early infancy	Hb ₄ (Barts)
2. HbH disease	-/- -/ α	Deletion of three		Severe, hemolytic α -genes	HbF(10%)
3. α -thalassemia trait	-/- α/α	Deletion of two α genes		Microcytic hypochromia but no anemia	Normal

D/d of microcytic hypochromic anemias

Test	Normal	Iron deficiency	Chr. ds	Thalassemia	Sideroblastic	Renal disease
1. Serum iron	50-150 μ g%	<30	<50	N, \uparrow	N, \uparrow	N
2. TIBC	300-360 μ g/dl	>360	\downarrow	N	N	N
3. % Saturation of Iron	30-50%	<10	10-20	30-80	30-80	N
4. Serum ferritin	50-200 μ g/L	<15	30-200	50-300	115-150	
5. Marrow iron stores	+ to +++	0	++++	-	Sideroblasts	+ to ++++
6. RDW	12-15%	\uparrow		N, \downarrow	\uparrow	
7. Retic count	<2%	\downarrow		\uparrow	-	

- Iron is absorbed almost exclusively in ferrous form mainly from **duodenum** & proximal jejunum
- In adult iron is distributed as----Mainly Hb (65%), transferrin (0.5%), heme and non-heme enzymes (0.5%)
- PBS** ----hypochromic and microcytic picture \downarrow MCV,
- BM/f**---- \downarrow Myeloid- erythroid ratio, micronormoblasts
- Lab/f**---- \uparrow TIBC, \downarrow Serum iron, \downarrow Serum ferritin, \downarrow Red cell protoporphyrin. **\downarrow IN THE SERUM FERRITIN LEVEL is the most sensitive and specific initial laboratory test for iron-deficiency anemia. Used for screening of IDA in community.**
- The response to oral iron therapy is observed by **reticulocytosis** which begins to appear in 3-4 days with a peak in about 10 days of starting t/t.
Day 1 \rightarrow Subjective improvement,
Day 2 \rightarrow Erythrocyte hyperplasia,
Day 3 \rightarrow reticulocytosis,
Day 4 -30 \rightarrow \uparrow in Hb
1-3 months \rightarrow Restoration of stores

- A \uparrow in Hb level by 0.5- 1 gm% per week is an optimum response to iron therapy. However iron therapy should be continued till normal Hb level is attained (for 1-3 mo. for t/t of deficiency and further 2-3 mo. to replenish the stores)

Differentiating points b/w IDA & Thal trait

Index	IDA	Thal trait (TT)
RBCs	<5 $\times 10^6$	
RDW	>17%	<14%
RDWI (RDW Index) = (MCV \times RDW)/RBCs	>220	<220
Mentzer's Index (MCV/RBC count)	>13.5	<11.5
Ferritin level	<10 μ g/L	>100 μ g/L
England - Fraser Index MCV + RDW - (RBC $\times 5 \times$ Hb)	>18.9	<18.9
Shine & Lal Index (MCV \times RBCs)	<u>≥ 1530</u>	<1530

- RDW & RBCs counts are most reliable in differentiating TT & IDA.
- Anemia in renal d/s (CRF) is non-proliferative anemia with normocytic normochromic picture.
- Helminthiasis causes MCHC anemia d/to iron deficiency.
- Microcytic hypochromic anemia with pallor & hepatomegaly but no splenomegaly indicates IDA.
- Anemia with pallor & hemolytic facies but no hepatomegaly, no splenomegaly, no lymphadenopathy favours a diagnosis of aplastic anemia.

- Pyridoxine deficiency causes sideroblastic anemia
- In lead poisoning --- Basophilic stippling with high serum lead
- Serum ferritin level is the most specific and most important lab/test to estimate iron stores.
- In iron deficiency anemia (IDA), first stage is negative iron balance (depletion of iron stores). When iron stores become depleted, the serum iron begins to fall. Gradually the TIBC ↑es, as the RBC protoporphyrin levels.
- Response to iron therapy is '↑ in reticulocyte count which begins 3-4 days after initiation of therapy.
- Macrophage iron is increased in anemia of chronic disease.
- Iron overload is seen in --- Thalassemia major, MDS, sideroblastic anemia, hemochromatosis, chronic liver diseases, multiple transfusion.
- Hemochromatosis is a disorder of iron storage where s. iron, % saturation of transferrin, s. ferritin all are ↑ed
- Plasma ferritin levels are reduced in ---- Iron deficiency, vitamin C deficiency, Hypothyroidism.
- Most sensitive index of iron deficiency anemia ---- ↓ Serum iron and ↑ TIBC

BETA THALASSEMIA

- NESTROFT test (Naked Eye Single Tube Red cell Osmotic Fragility Test) is a simple and rapid screening test for diseases with ↓ OF e.g.
 - β -Thalassemia major
 - IDA (Iron deficiency anemia)
 - Liver d/s
 - Hemoglobinopathies
- On other hand in hereditary spherocytosis, OF is ↑ ed.
- Mentzer's index is ratio of MCV/RBC count. Value < 13 favors thalassemia & if it is >13 IDA is more likely.

- β thalassemia is quantitative defect in Hb synthesis. There is diminished synthesis of β-globin chain with normal α chain.
- Hb electrophoresis is diagnostic

- Hemolytic anemia, splenomegaly+
- BM hyperplasia (large no. of late and intermediate normoblast i.e. erythroblast are characteristic)
- Lab/d : based on HbF estimation & β-globin chain synthesis ratio.

HbF

- ↑↑ HbF is seen in --- β thal major/trait, HbSS, HbSC, preterm infants treated with recombinant erythropoietin, aplastic anemia, hematological stress.

HEMOLYTIC ANEMIA

Common to all hemolytic anemias

- Hemosiderinuria
- ↑ K⁺ (hyperkalemia)
- ↑ Serum LDH
- ↑ Unconjugated bilirubin
- ↑ Urobilinogen in urine (high colored / lemon yellow)
- ↓ or absent Haptoglobin, hemopexin
- Splenomegaly, reticulocytosis
- Serum iron levels high, ↓ TIBC, ↑ed iron stores
- Erythroid hyperplasia (expansion of marrow space, bossing of skull).

- Hemoglobinuria, hemosiderinuria, bilirubinuria are features of intra-vascular hemolysis.

MICRO-ANGIOPATHIC HEMOLYTIC ANEMIAS

- Seen in vessel disease (fragments⁺⁺⁺, hemolysis⁺, thrombocytopenia⁺) secondary to intravascular trauma.
- Causes are : malignant HTN, eclampsia, hemangioma, immune diseases (Scleroderma), renal graft rejection
- Schistocytes present (specific)
- 3 mechanisms are responsible

External impact	Cardiac hemolysis	Fibrin deposit in microvasculature
- Direct trauma over bony	In prosthetic valve recipients	- TTP / HUS / DIC
- March hemoglobinuria		- Disseminated cancers.

Auto-immune Hemolytic anemia (AIHA) :

- Use of Direct Coomb's test in diagnosis causes of AIHA-

Reaction with	Coomb's +ve AIHA		
Anti IgG	+	+	-
Anti C ₃	+	-	+
Examples	Antibodies to glycoprotein antigen e.g. SLE	Ab to Rh antigens, Hemolysis by α -methyl dopa, or penicillin	Cold reacting Ab (Donath-Landsteiner antibody) drug reactions, complement activation by immune complexes

- Warm AIHA and cold agglutinin d/s are m/c among adults over age 50, in whom the diseases are usually chronic and relapsing; PCH, a rare disorder occurring most commonly in children, usually resolves on its own.

Cold antibodies type AIHA

- Antibodies that react with polysaccharide antigens are usually IgM & react better at temperature $<37^{\circ}\text{C}$. [Very rarely antibodies are IgG (the Donath Landsteiner's antibody of PCH).
- In chronic cold agglutinin d/s : cold-activated immunoglobulin M (IgM) and complement (C3d) coat RBCs and trigger hemolysis.
- Patients are usually over age 50; sometimes resolves with cold avoidance; rarely progresses to renal failure
- Causes are:
 - Polyclonal antibodies in acute infections :
Acute (Black water fever, trypanosomiasis), Mycoplasma (Anti - I), Infectious mononucleosis.
 - Lymphoma, idiopathic
- Cold hemolysins are IgG (the Donath Landsteiner's antibody of PCH).
- Paroxysmal cold hemoglobinuria (PCH): rare d/s induced most often by postviral Donath-Landsteiner autoantibody at cold temperatures in children. Often acute and severe, though usually short-lived and self-limited. Rarely progresses to renal failure, frank lymphoma, or death.

- Seen in tertiary syphilis, Paroxysmal cold hemoglobinuria PCH (Anti - p)
- IgG antibody, Donath-Landsteiner antibody (Vs. P blood group antigen)

Warm antibodies type AIHA

- In warm AIHA , autoantibody IgG attacks RBCs.
- Patients are usually 50 yr + females.
- Causes are :
Immune system neoplasms like Lymphoma (CLL, NHL, HD), SLE, Drugs (α -methyl dopa, quinidine, penicillin), Post viral
- Direct coomb +ve, IgG antibody type.
- Most severe form is a/w hemolysis , hemoglobinemia, hemoglobinuria with shock.
- Typically treated with corticosteroids and therapies for underlying diseases

→ Coomb's +ve AIHA is also seen with Rmp, INH, co-trimoxazole.

→ AIHA may be a/w leukemia esp. B-cell type CLL and NHL

G-6-PD deficiency

- M/c hereditary enzyme deficiency worldwide inherited as X-LINKED RECESSIVE
- Defect in HMP shunt
- NADPH is not generated so RBCs are exposed to oxidant stress
- Provides protection against falciparum malaria
- D/g by met-Hb reduction test

Pyruvate kinase def.

- A-R INHERITANCE, Defect in EMP/ glycolytic path

Hereditary spherocytosis (HS)

- HS is inherited as AD
- M/c membrane defect is ankyrin. Spectrin defects are also seen
- C/F
Massive splenomegaly with anemia, jaundice and gall stones
- Lab/F --- \downarrow MCV, \uparrow MCHC, osmotic fragility is \uparrow (Remember: High Of in HS)

- T/t

TOC is splenectomy (Splenectomy eliminates risk of max^m hemolysis ; may be delayed upto age of 4 years)

- CI/v--A 40 year old female with history of jaundice and pallor for past 1 month shows a large number of spherocytes in her peripheral smear.

The most likely diagnosis is---Hereditary spherocytosis

The most relevant test for diagnosis would be---Osmotic fragility test

MEGALOBLASTIC ANEMIA

- *Imp. causes are ---*

- Vitamin B₁₂ deficiency, Folic acid deficiency
- Orotic aciduria
- Liver diseases
- Hypothyroidism
- Drugs (N₂O inhalation, phenytoin, primidone, phenobarb, folate antagonists viz. Mtx, cotrimoxazole, pentamidine etc.)

- **Vitamin B₁₂ deficiency** is usually an AR genetic disorder called "**pernicious anemia**" or Addisonian anemia.

It may also occur in short bowel syndrome, ileal resection/ atresia, blind loop syndrome and fish tapeworm (*Diphyllobothrium latum*) infestation.

In pernicious anemia there is deficiency of intrinsic factor (IF) and achlorhydria

- **Folic acid deficiency** is usually seen in tropical sprue, malnutrition, malabsorption, anticonvulsants therapy, in short bowel syndrome, anticancer drugs, goat's milk consumption

- *CI/f* --- Periungual or knuckle pigmentation , chronic diarrhoea in FA deficiency

- *Lab/f* --- **Hypersegmented neutrophils**, ↑ LDH , giant platelets

- *T/t* --- It is advised to give Vitamin B12 and folic acid concurrently because t/t with folate alone may improve anemia but leads to progression of neurologic d/s

→ *Macrocytosis without myelocytes is seen in --- Tropical sprue*

→ *Giant platelets are seen in --- Megaloblastic anemia, essential thrombocytosis, myeloid metaplasia*

→ *Small platelets are seen in --- Bernard solier d/s (half size)*

OTHER ANEMIAS

Anemia of Chronic d/s

- Normal Hb structure with ↓ Hb content.
- ↑ Marrow iron stores.

Hemoglobinopathies

- Change in Hb structure with ↓ Hb content.
- Hb- D of Punjab :

SICKLE CELL DISEASE (SCD)

Autosomal recessive disorder c/by hemolytic anemia and sickling crisis

- Glutamate is substituted by valine in 6th beta chain of globin
- On deoxygenation 2nd sticky patch (or hydrophobic patch) is generated as result of replacement of polar (glutamate) residue with a non-polar (valine) one
- HbS is produced. Heterozygotes for HbS are protected from malaria.
- Normocytic normochromic Anemia
- Howell- Jolly bodies, target cells are +nt.
- Recurrent jaundice. Cholelithiasis is common (but Urolithiasis is uncommon)
- Pulmonary arterial HTN (CCF)
- Renal papillary necrosis⁺ hematuria
- Bone pain is m/c feature in children (**Hand-foot syndrome**)
- Priapism
- *In adult*: Acute chest syndrome (d/to mycoplasma)
- Gamma-Gandy bodies⁺,
- **Auto-splenectomy**
- Leucocytosis, thrombocytosis, hyperplastic marrow.
- Rx: **Stem cell transplantation** in utero without genetic modification is TOC for SCA.

Hand foot syndrome (or dactylitis)

- Is a c/c of SCD. Presents as bone pain in children.

Hand foot and mouth d/s

- Is a viral infestation a/w rashes.
- M/c caused by coxsackie virus A16 but may be caused by other coxsackie viruses like A 5,7,9,10 and B 2,5 etc.; enterovirus 71.
- A similar infection is herpangina.

FANCONI ANEMIA

- Pure red cell aplasia is seen with Parvo B19, HIV, EBV, HTLV-1.
Giant pronormoblasts are seen in BM (bone marrow).

Low retics c/b seen in

- Aplastic anemia
- Pure red cell aplasia
- Fanconi's anemia

Pancytopenia with cellular marrow c/b seen in

- Megaloblastic anemia
- CDA (Congenital dysplastic anemia)
- Myelodysplastic anemia

FANCONI ANEMIA

- AR inheritance
- Abnormal chromosomal fragility. Cell fusion of Fanconi cells with normal cells produces a correction on chromosomal fragility, a process called complementation.
- ↓IL-6 ↑↑↑ TNF α , ↑AFP ↑HbF
- Hyperpigmentation of skin, short stature, absent radii, hypoplastic/ absent thymus, underdeveloped penis, undescended / absent/ atrophic testes, mental retardation
- Lab/f: Pancytopenia --- thrombocytopenia, granulocytopenia, macrocytopenia. Hypocellular and fatty marrow
- C/c: Increased risk of head, neck cancers.
- T/t : G-CSF

→ Pancytopenia with hypocellular and fatty marrow is seen in → Fanconi anemia

→ Pancytopenia with hypocellular marrow c/b seen in → PNH

→ Pancytopenia with plasmacytosis and acellular marrow is seen in → Aplastic anemia

DISORDER OF BLEEDING & COAGULATION

PNH (Paroxysmal Nocturnal Hemoglobinuria)

- Acquired intracorpuscular hemolytic anemia ch/by triad of complement induced hemolytic anemia + hemoglobinuria + thrombosis
- Etiopatho:
 - Mutation in PIGA gene
 - RBCs are deficient in DAF (CD55) and protectin (CD59).

& become susceptible to complement mediated lysis (during sleep mild respiratory acidosis occurs which leads to hypoxia, activation of complements → Red cell lysis → nocturnal hemoglobinuria in 25% patients).

◦ Cl/f:

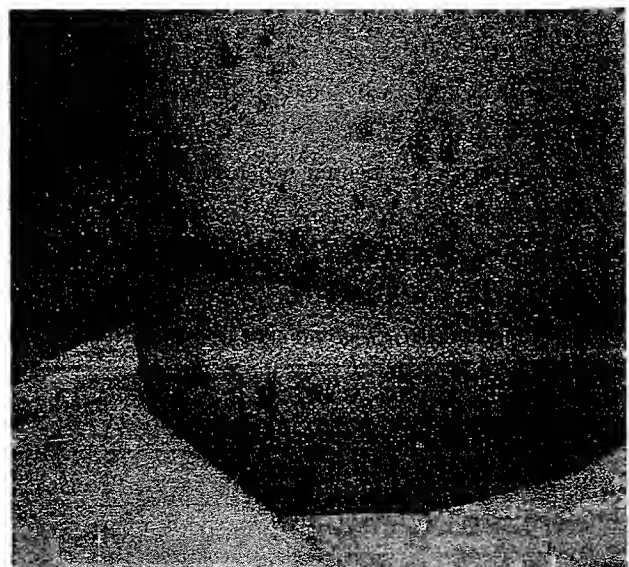
- Esophageal spasm, erectile dysfunction and pain abdomen are attributed to binding of Hb with NO.
- Venous thrombosis
- Pancytopenia, complement mediated thrombocytopenia.

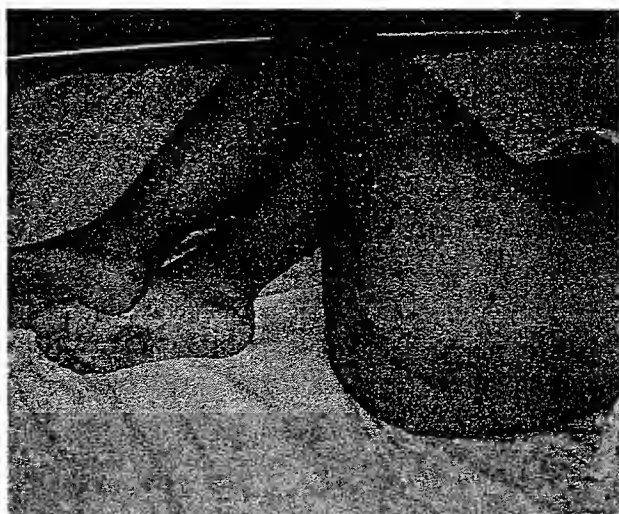
◦ Lab/f:

- ↓ LAP - score
- Gold standard for Dx is : Flow cytometry of granulocytes and erythrocytes - evaluate for presence of GPI-linked antigens . Flow cytometry is also most sensitive & specific test.
- Coomb's negative AIHA --- congestive splenomegaly, intermittent hemoglobinuria , hemosiderinuria, ↑ LDH
- BM :- Patients with hemoglobinuria are more likely to have a large PNH clone and hypercellular bone marrow BM is hypocellular only when a/w aplastic anemia.
- Screening tests - Ham's test. & Sucrose lysis test (more sensitive)
- Paroxysmal & nocturnal intravascular hemolysis occurs only in 25% patients, remaining 75% patient present with chronic hemolysis without hemoglobinuria.
- T/t :- Cyclosporine & ATGH (Anti T-cell therapies) + steroids.

HSP (Anaphylactoid Purpura) :

- Commonest presentation is palpable purpura limited to buttocks & lower extremities.
- Self limiting hypersensitivity/ leukocytoclastic vasculitis which involves small and medium sized v/s.





Photograph : Lesions in HSP

- M/c form of vasculitis in children (M>F)
- Cl/f
 - **Abdominal pain, blood in stool (Melena)** is characteristic.
 - Past H/o Atopy
 - **Arthralgia** non-migratory (Knee/ankle)
 - Palpable purpura, pruritic rashes (Centrifugal)
 - Renal involvement in 40% of the patients. Nephritis is *Burger's disease type (In children) & RPGN type (In adults)*
- Lab/F
 - Normal platelet count.
 - All coagulation test normal
 - Circulating immune complexes (IgA₃+Fibrin) deposited in vessel walls.
 - Mild leucocytosis (leukocytoclastic reaction) & **IgA elevated**
 - ANCA -ve vasculitis
- T/t - glucocorticoids

DIC

- Fibrinogen level correlates with severity of disease/bleeding.
- **Important causes** :- Rocky mountain spotted fever, Malaria, Histoplasma, Aspergillosis, Acute Promyelocytic leukemia (M₃ type AML), Liver ds., heat stroke, Polycythemia vera, Extensive surgery.
- **Obstetric causes** : IUD, amniotic fluid embolism, retained placenta, abruptio placentae
- M/c symptom: - Bleeding.
- Lab/F :-
 - Thrombocytopenia (↑BT)
 - Microangiopathic hemolytic anemia

All coagulation tests are increased except fibrinogen level

↑ in PT, APTT (CT), TT, D-dimer and FDP ↑↑

↓ in Fibrinogen level & Euglobulin lysis time

- Site of thrombosis in DIC → Brain > Heart > lung > kidney
- In Acute DIC Bleeding c/c are more.
In chronic DIC (cancer induced) thrombotic c/c are more.
- T/t - Cryoprecipitate
- DIC does not occur in nephrotic syndrome and there is hyperfibrinogenemia.

HUS

- 2 types
 - D+ HUS** : M/c form in children, pathogenic agent is the shiga toxin (verotoxin) produced by STEC E.coli. O157; H7 is the m/c strain.
 - D- HUS** : Non Shiga toxin associated HUS. These atypical HUS (aHUS) are caused by congenital complement dysregulation. ↓ C3 levels. M/c cause is deficiency of factor H.
- Pathogenesis of childhood HUS involves both thrombosis and vasoconstriction (thrombotic microangiopathy).
- D+ HUS : >80% cases precede within a week of bloody diarrhoea. A/w abdominal pain, cramps, & vomiting. Fever is typically absent. Neurological symptoms are common.
- Coomb's negative hemolytic anemia and micro-angiopathic hemolytic anemia (MAHA). Disintegrin & ↓ADAMTS13 are found.
- Acquired vascular bleeding disorder (irregularities of renal vascular endothelium)
- D/d

Features	HUS	TTP
Hb	↓	↑
Retics	↑	↑
Platelets	↓	↓
PT/APTT	Normal	Normal
RF/ANA	- ve	+ ve in 20%
CNS symptoms	Less	Common
Renal failure	+	-
Age group	< 5 yr	3rd/4th decade
Prognosis	Self limiting	High mortality
T/t	Supportive	Curative

- **Thrombocytopenia** occurs (other coagulation tests normal)
- Helmet cells & Burr cells, reticulocytosis, ↑ LDH, hyperkalemia in blood.
- Hyaline thrombi in endothelium of kidney, ARF
- Unconjugated Hyperbilirubinemia, Hemosiderinuria.
- T/t is supportive only. Antibiotics should NOT be used.

THROMBOCYTOPENIA

ITP

C/P	Acute ITP	Chronic ITP
Age group	2-6 yr	Any age
Onset	Acute	Insidious
Preceding illness, association	Viral infections, URI	SLE, RA, AIDS, Auto-immune thyroiditis
Spleen size	Normal	May be normal
Complication	Rare	Intra cranial bleed
T/t	Supportive	Curative

- PBS : ↓ in no. of platelets with relatively large forms seen
- BM : ↑no. of megakaryocytes.
- Petechiae, purpura, mucosal bleeding.
- Abnormally prolonged BT
- *Spleen is usually not palpable*
- Poor clot retraction is diagnostic
- *Rx in Adults :*

Large doses of steroids (prednisolone orally)
or in failed cases → splenectomy.

Platelet concentrates (for life threatening bleeding or platelet counts <10,000).

- *Rx in children :*
 - Acute ITP is usually self-limiting.
 - Oral prednisolone (2 mg/kg) ↑ platelet counts in 3-4 days.
 - **IVIG** (or Anti-D / Anti-Rh antibodies) are indicated if there is :-
 - A) Risk of life threatening bleeds (ICH, G.I. h'mge, severe menorrhagia etc.)
 - B) If platelet count < 10,000 with minor purpura or counts < $20 \times 10^9/L$ with mucosal bleed in children.
 - **Splenectomy** is the definitive T/t. It is indicated in symptomatic patient with chronic ITP. or in case of failure of above T/t in acute ITP.

- Spontaneous bleeding or Platelet counts < 10,000 is an indication to start platelet transfusion.

TTP

- There is deficiency of vWF metalloprotease (**ADMTSβ**)
- Microangiopathic hemolytic anemia
- Thrombocytopenia, Hyaline microthrombi throughout body, purpura (Hence the name TTP). **Thrombus is platelet rich.**
- Neurological symptoms are common.
- Renal dysfunction.
- **Splenomegaly**
- Fever.
- Rapid onset, *fulminant course (fatal)*
- BM : Megakaryocytes normal or ↑
- *Death is d/to intracerebral h'age*
- **Lab/f** : Coomb's -ve hemolytic anemia with schistocytes, leucocytosis.
- D/d : APTT, PT are normal in In TTP while these are abnormal in DIC
- Level of platelet IgG & C normal
- Gingival biopsy +ve (30-40%)
- Rx. : Use of exchange transfusion, **intensive plasmapheresis (curative)** coupled with infusion of FFP, Glucocorticoids.

→ *Evan's syndrome is ITP + AIHA. Seen in pregnancy. Most of the patient remain asymptomatic.*

→ *HELLP syndrome is elevated liver enzymes with thrombocytopenia in pregnancy.*

Thrombocytopenia

Immunologic (Coomb's positive)	Non-immunologic (Coomb's negative)
<ul style="list-style-type: none"> • ITP • CVD (SLE, DLE) 	<ul style="list-style-type: none"> • DIC • TTP • HUS

Platelet Defects

Abnormality of platelet	Seen in
• Aggregation	Glanzman's thrombosthenia
• Adhesion	vWD Bernard Soulier's syndrome
• Secretion (α granules)	Grey platelet syndrome
• Secretion (Dense granules)	Chediak Higashi syndrome, Wiskott's Aldrich Syndrome, TAR syndrome

Interpretation of coagulation tests

Plat. count	BT	aPTT	PT	TT	Fibrinogen	FDPs	Possible cause	Example
↓	N, ↑	N	N	N	N	↓	↓ production, sequestr ⁿ	Radiation, C _T splenomegaly
N	↑	N	N	N	N	N	Platelet dysfunction	Drugs (ASA, NSAIDS, clopidogril, uremia)
N	↑	↑	N	N	N	N	Severe vWF def	vWD
N	N	↑	N	N	N	N	Factor deficiency, Factor inhibition	Low dose heparin, poor collec ⁿ
N	N	N	↑	N	N	N	Factor VII def.	Early liver ds/ vitK deficiency
N	N	↑	↑	↑	N	N	Multiple factor def.	Late liver ds/ late coumarin def, heparin
↓	↑	↑	↑	↑	↓	N	Dilution of factors/ platelets	Massive transfusion
↓	↑	↑	↑	↑	↓	↑	Hypercoagulable state. ↓ produc ⁿ of factors	DIC, advance liver ds

COAGULATION DISORDERS

D/s	F/def	Mode	BT	CT (APTT)	Remark, T/t
Hemophilia A (Classic h~)	VIII	XR	N	↑↑	F VIII concentrates, EACA
Hemophilia B (Christmas ds)	IX	XR	N	↑	Cryo (FFP, factor IX)
Hemophilia C	XI	AR	N	↑	M>F
Parahemophilia (Owren's d/s)	V	AR			Both M, F affected
vWD (Pseudo-hemophilia)	VIII + vWF	AD	↑↑	↑	FFP, F VIII, desmopressin

- **Hemophilia A** : Spontaneous bleeding not common but when active bleeding start hemostasis is not achieved Patients are always male as it is transmitted as a X-linked recessive trait. Platelet counts are normal or raised.

- **Hemophilia B** : Also k/as Christmas d/s.

- vWD is char/by decreased/defective vWF which is a/w secondary decrease in factor 8
- Correction of APTT with normal serum goes in favor of hemophilia B.
- Correction of APTT with adsorbed plasma (& not with normal serum) in favor of hemophilia A (factor VIII deficiency)
- Among the clotting factors, factor XII deficiency, does not produce bleeding but thrombosis.

Coagulation tests :

↑APTT (or PTT)	<ul style="list-style-type: none"> • Screens intrinsic path defect • Reflects clotting time (CT) in general • Heparin at low concentration • ↑APTT is seen in def. of <ul style="list-style-type: none"> - Factor 11, 12, HMWK (with no bleeding) - Factor, 8, 9 (with severe bleeding)
↑PT	<ul style="list-style-type: none"> • Screens extrinsic / tissue factor dependent pathway <ul style="list-style-type: none"> - Warfarin therapy - Early vit, K deficiency - DIC, Liver ds. - Factor 7 & 5 Def.

↑APTT & ↑PT	<ul style="list-style-type: none"> • Screens common pathway after activation of factor X -Heparin therapy (at high concentration) -Factor 1, 2, 5, 10 def. -Vit. K. def. (late)
↑↑Thrombin Time (TT)	<p>A specific test for conversion of fibrinogen to fibrin)</p> <ul style="list-style-type: none"> • ↑ in afibrinogenemia • After heparin treatment • DIC
↑BT	<p>Conditions which inhibit platelet plugging</p> <ul style="list-style-type: none"> • Aspirin ingestion • Qualitative dysfunction of platelet • VWD, Thrombocytopenia • Renal ds (multiple myeloma) • Scurvy

- Clot solubility test in 5M urea is performed for factor 13 deficiency/defective cross-linking
- Rapid clot lysis for α-2 plasmin inhibitor
- Parahemophilia is d/to factor 5 deficiency
- Oral anticoagulant therapy is monitored with PT.

Myelodysplastic Synd. , Myeloid Metaplasia

	Myelodysplastic syndrome	Myeloid metaplasia with myelofibrosis
Also k/as	Dysmyelopoietic syndrome (Pre Leukemic syndrome)	-
Age group	> 50	
A/w	Radiation, chemo	Agnogenic; PV (25%), CML, irradiation
↑ Risk of	Transform in AML (5-20%)	
Cause	Hematopoiesis in marrow in varying combinations	Proliferation of neoplastic stem cells outside BM (Shift of hemopoiesis in liver/spleen/LN)
C/F	Anemia : dimorphic (Megaloblastic / nuclear erythroid precursor)	Massive hepatosplenomegaly, portal HTN, jaundice, ascites, bone pain
Lab/F	Ring sideroblasts <u>Pseudo-Pelger heut anomaly</u> Hypolobated megakaryocytes	↑TLC, platelets, Giant platelets, Tear drop cells Fragmented & immature RBCs, Dry tap in BM biopsy
T/t	-	T/t : Hydroxyurea, IFN-α, Anagrelide

MYELOPROLIFERATIVE DISORDERS (MPD)

Polycythemia Vera (PV)

- JAK2 exon 12 mutation
 - ↓ESR and ↓ or -nt erythropoietin
 - Normal arterial SpO₂ rest all ↑ed
 - ↑ TLC (leucocytosis)
 - ↑ Red cell mass and Hct → ↑Viscosity → ↑ Systolic BP
 - ↑ Platelets ↑ Spleen
 - ↑ turnover of Hct → ↑Serum LDH, Uric Acid
 - ↑↑LAP score
 - Histamine release → itching.
 - Neurological symptoms (headache, vertigo, tinnitus)
 - Bleeding from GIT, epistaxis
- Chronic myeloproliferative disorders are:
- PV, idiopathic myelofibrosis, essential thrombocythosis and CML
- Tumours a/w PV are — RCC, cerebellar hemangioblastoma, HCC or hepatoma, pheochromocytoma, meningioma

Essential Thrombocythosis / Thrombocythemia :

- Myeloproliferative disease characterized by ↑↑↑ platelet count without any recognizable stimulus
 - Platelet aggregation within microcirculation results in arterial/venous thrombosis, easy bruising, and TIA/Stroke
 - Platelet count >4 lacs/μL
 - Large platelets/hyperdiploid cells, megakaryocytic fragments present
- Since 1/3rd of platelet mass is normally sequestered in the spleen, splenectomy will ↑se the platelet count by 30% and vice versa splenomegaly (as in lymphoma, leukemia, MPS) leads to 2nd thrombocytopenia .
- Secondary / Reactive thrombocytosis is seen in -- Chronic infection, chronic iron deficiency, Post-splenectomy, RA

LEUKEMIAS

- M/c type of ALL --- CALLA +ve, tdT +ve ALL (Pre B-cell leukemia).

- Commonest leukemia age wise
In children <15 year (ALL),
15-40 year (AML),
40-60 year age group (AML & CML),
in elderly >60 year (CLL)
- ALL is the m/c leukemia in children and overall m/c malignancy of children
- CLL is most common leukemia overall, Most insidious onset.
- Most malignant behavior or worst prognosis is seen in AML (esp M₁) > ALL > CML > CLL
- In AML blasts are +ve for MPO and -ve for Sudan black but in ALL it is opposite i.e. MPO -ve and Sudan black +ve.
- Smear cell +nt in ALL & CLL. Smudge cells +nt in CLL
- Aleukemic leukemia: seen in AML & ALL
- A blast count >30% indicates acute leukemia whereas <30% blasts in the marrow indicates chronic leukemia.

ALL

- *Prognostic factors for ALL are*

Determinants	Favourable	Unfavourable
• Age in yr	2-8	<1 and >10
• TLC	<20,000	>1 lac
• Cytogenetics	Hyperdiploidy, trisomy	hypodiploidy, Ph chromosome
• Translocation	TEL/AML1 genes re-arrangement	9:22; 4:11
• Immunophenotype	Early pre B-cell	T cell
• FAB type	L1	L2,3
• DNA index	>0.16	<0.16
• Minimal residual d/s	<10 ⁻⁴	>10 ⁻³
• HSM, LN, testicular enlargement	-	+
• CNS involvement	-	+(blasts, pleo)

- *Favourable prognostic factors are*
 - Hyperdiploidy, trisomy
 - A rapid response to t/t,
 - Rearrangements of the TEL/ AML1 genes
 - Age b/w 1 to 10 years
 - Female sex
- **Metaphyseal translucencies** are the earliest & most characteristic features of childhood leukemia.

AML

- AML is a/w Down, Patau, Klinefelter's, ataxia telangiectasia, Fanconi anemia, sideroblastic anemia.
- Auer rods are seen in AML arising from myeloblasts

(Auer rods are not seen in CML and monocytic type of AML).

- Leukemia developing in myelodysplastic syndrome --- AML
- Normal cytogenetics, deletion of X or Y, translocations t (8: 21), t (15:17) and mutated nucleophosmin has a favourable prognosis.
- CD34+, TdT positivity, FAB type M0, M6, M7; presence of dysplastic megakaryocytes, monosomy has a poor prognosis.

AML Types

Type	AML	Cytogenetics	Clf, Cytochemistry
M ₁	Immature type	t(9:22), Philadelphia chr.	MPO, SB +
M ₂	AML with maturation M/c type	t(8:21)	Chloroma ⁺
M ₃	Acute promyelocytic leukemia (APL)	t(15:17), Multiple Auer rods	<u>DIC is common</u>
M ₄	Myelomonocytic Naegeli type	Inversion 16,3,7 3q rearrangement	Good prognosis <u>LN-pathy, eosinophilia</u>
M ₅	Monocytic Schilling type		Gum hypertrophy Organomegaly LN-pathy, skin infiltration
M ₆	Erythrocytic Erythro-leukemia	Glycophorin +ve	Old age <u>Megaloblastic anemia is seen</u>
M ₇	Megakaryocytic		Antibody Vs. VWF Myelofibrosis

Marker enzymes in leukemia

Leukemia	MPO	Sudan B black	NSE or chloroacetate esterase	TRAP	PAS
• AML	+	+/-	+ in M4,5	-	FA
• ALL	-	+	-	-	+
• CML	-	-	-	-	-
• HCL	-	-	-	+	-
• CLL	-	-	-	-	+

Leukocyte Alkaline Phosphatase Score (LAP score)

- LAP scores are typically low in **CML** but score ↑es during blast crisis or acceleration phase. Low LAP score are also seen in PNH
- LAP is high in --- Polycythemia, leukemoid reaction, infection.

CLL

- In typical B cell CLL, trisomy 12 conveys a poorer prognosis.
- Only leukemia with thrombocytosis ---CML (↑ Platelets, ↑Neutrophils, Eo, ↑baso)

CML

- A/w massive splenomegaly
- Only leukemia with thrombocytosis ---CML (↑ Platelets, ↑Neutrophils, Eo, ↑baso)
- In CML sometimes the symptom is a dragging sensation in abdomen due to extreme splenomegaly.
- *Prognostic factors for CML identified in*

Chemotherapy treated patients (Sokal Index) *α-IFN treated patients (Hasford System)*

- | | |
|-------------------------------|-----------------------------------|
| 1. Spleen size | 1. Age |
| 2. % of circulating blast | 2. <u>Spleen size</u> |
| 3. Platelet count | 3. % of circulating blast |
| 4. Cytogenic clonal evolution | 4. Platelet count |
| | 5. % of eosinophils and basophils |

- Persistent splenomegaly despite continued therapy is a sign of disease acceleration
- Lymphadenopathy if present p/g is poor
- Ph chromosome is associated with poor prognosis
- PAS +ve myeloblasts, promyelocytes and erythroblasts are seen in ALL (but TdT and B-cell markers may be +ve in CML)
- Serum levels of vitamin B12 and vitamin B12 binding capacity is increased
- Blood smear reveal extramedullary hematopoiesis (hepatosplenomegaly) tear drop cells, nucleated red cells, myelocytes and promyelocytes
- Dry tap in BM aspiration
- ↑LDH and ↑ALP
- Splenic infarcts may be present
- Risk of developing acute leukemias having aggressive course

Juvenile CML:

Usually presents in children below 2 yr. Erythrocytes have fetal characteristics like Hb-F, *i-antigen score*.

Not a/w Philadelphia chromosome.

- DOC for CML: Dasatinib > Imatinib

Hairy Cell Leukemia (HCL)

- B-cell neoplasm d/to EBV.
- Monocytopenia, *massive splenomegaly*, vasculitis
- Cause of death : Legionella pneumonia
- D/d from CLL : HCL is **TRAP +ve** (Tartrate resistant acid phosphatase), **CD25 +ve & CD 103 +ve**.
- BM : Is very hypocellular but not dysplastic. Large aggregates of CD20 + lymphocytes are present.
- Splenic red pulp MC site of neoplastic proliferation.
- T/t : Cladribine (other useful drugs: Pentostatin, α-IFN)

LYMPHOMA

MYCOSIS FUNGOIDES :

- Also k/ as “cutaneous T-cell lymphoma”.
- Involves CD_4^+ T-helper cells
- Involves skin, LN and other organs (Dermatopathic lymphadenopathy).
- When neoplastic cells enters peripheral blood stream it is k/as **Sézary syndrome**. In which **total skin electron irradiation (whole body radiation therapy)** is given.
- In skin “**Pautrier’s microabscesses**” are seen.

→ *Granulomatous microabscess are seen in a lymph node in cat scratch d/s caused by Bartonella henselae.*

HODGKIN'S DISEASE (HD or HL)

- **Reed Sternberg cells** (RS cells) are hallmark of HD. They are neoplastic T or B lymphocyte cell origin and have characteristic “Owl eye appearance”.
- M/c type of HD is **nodular sclerosing** type but in India mixed cellularity type is more common.
- M/c type of HD in females is nodular sclerosing type other types are more common in males.

◦ Rye classification of HD stage :

Features	Cell type	RS cell	Lympho	Prognosis
Lymphocyte predominance	Popcorn cell (Polypoidal)	+	++++	Best
Nodular sclerosis	Lacunar cells	++	+++	V. good
Mixed cellularity	Monocuclear type RS cell (Classic)	+++	++	Good
Lymphocytic depletion type	Sarcomatous or pleomorphic RS cell	++++	+	Worst

- Mediastinal involvement is common in nodular sclerosing type .
- HD patients usually present in stage IIA.
- T/t of HD stage :
IA, IIA (Localized ds) → Radiation.
Stage IIB-IV → Combination chemotherapy with ABVD regimen (Adria-, Bleo-, Vinc-, Darcarb-)

- Other conditions having RS cells ----- IM, Mycosis fungoides.
- Prognosis of HD depends upon ----- Staging.
- Nodular sclerosis is ----- M/c, M/c in females, M/c involvement of mediastinum.
- Lymphocytic and histiocytic variants (L+H) of RS Cell are seen in lymphocytic predominance type of HD.

Hodgkin's Disease Vs. NHL

HD	NHL
◦ Bimodal peak in 20's & 50's (involves younger people)	◦ Usually involves elderly
◦ B-symptoms are common Fever, night sweats, weight loss	◦ Rare
◦ Localized LN pathy	◦ Generalized LN pathy
◦ Contiguous spread to LN	◦ Random spread to LN
◦ Less	◦ Involves Waldeyer's ring, skin, GIT.

NON HODGKIN's LYMPHOMAS (NHL)

◦ Classification

- Rappaport's - based on pattern and size of cell (nodular and diffuse)
- Leukes-collins classification - based on marker study
- Working formulation - based on natural history and response to T/t.

◦ Prognosis :

- Nodular have more favorable than diffuse
- Lymphocytic (small cells) have more favorable than histiocytic (larger cells are called histiocytic)
- M/c extranodal site of primary malignant NHL is stomach (H.pylori associated low grade B-cell MALT lymphomas).

- NHL resembling CLL -- Small lymphocyte & lymphocytic lymphoma (B-cell NHL)
- NHL resembling ALL -- Lymphoblastic lymphoma (T-cell malignant lymphoma)
- NHL producing mediastinal lymphadenopathy -- T-cell lymphoblastic ALL
- Overall M/c type of NHL -- Follicular centre cell lymphoma, small cleaved type
- M/c type of NHL in children--Burkitt's lymphoma
- M/c NHL in AIDS patient -- Immunoblastic lymphomas (primary CNS lymphomas)

Burkitt's Lymphoma

- B-cell lymphoma
- It was initially seen in African adolescent boy as jaw tumours. It may spread to extranodal sites such as bone marrow and CNS (meninges may be involved) and peripheral lymphadenopathy and or intraabdominal mass are seen.
- It is a high grade small non-cleaved, lymphocytic lymphoma. It has high mitotic (proliferating) activity. It is one of the fastest growing neoplasm.

- M/c site is *abdominal cavity* (Payer's patches of small intestine in boys and pelvic cavity in girls)
- A/w EBV, translocation t (8:14) mainly ; sometimes t (2:8) or t (8:22).
Express surface IgM, germinal center B-cell markers CD19, CD20, CD10 and BCL6, CD21+ ve in Africans
- On microscopy "Starry sky pattern" is seen in which macrophage form stars.
- T/t: Should begin within 48 h of d/g and involves extensive chemotherapy using cyclophosphamide.
Prophylactic CNS irradiation/ chemo is mandatory.

HISTIOCYTOSIS-X

(Langerhans cell Histiocytosis)

- 3 diseases are included in H~
 - Eosinophilic granuloma (MC & benign form).
 - Hand Schüller-Christian disease
 - Litterer-Siwe disease (most aggressive form).

Features	Eosinophilic granuloma	Hand Schüller Christian Disease	Letterer Siwe disease
M/c site	Skull	Skull	Diffuse
Bony lesion	Unifocal lytic	Multifocal lytic	Multifocal cystic
M/c	Commonest form	-	Aggressive d/s
Characteristic	Geographical skull (punched out lucencies in skull vault) Vertebrae (single vertebra plana) pelvis, femur	Triad of Lytic lesions in skull (Calvarial bone defect) + Exophthalmos + DI	Diffuse eczematous rash Splenomegaly, Pancytopenia.

→ Eosinophilic granuloma is the m/c cause of single vertebral body collapse in a child with intact disc space (single vertebra plana)

- All histiocytosis cells are CD_{1a} positive and Langerhans cells are HLA DR +ve
- Characteristic of all H~ : **Langerhans' granules** (They have Tennis Racket appearance) or Hx Bodies (**Birbeck's granules**)
- Histiocytes (modified macrophages) have coffee bean nuclei

MULTIPLE MYELOMA (MM)

- Also k/as plasma cell myeloma.
- Classical triad in D/g.
Marrow plasmacytosis + Lytic bone lesions + Serum or urine M-component
- Alkaline phosphatase level is **normal**
↑ESR, hypogammaglobulinemia, hypercalcemia are characteristic findings
↑ Urea/creatinine, & uric acid, A/G ratio reversed.
- Criteria for D/g: Presence of 1 major + 1 minor or at least 3 minor criteria in symptomatic and progressive pt.

Major :

1. Plasmacytomas on tissue biopsy
2. Marrow plasmacytosis with >30% plasma cells
3. Monoclonal globulin (M protein) spikes on serum electrophoresis.
>3.5 for IgG and >2g/dL for IgA; 1 g/d of κ or λ light chain excretion on urine electrophoresis in the -nce of amyloidosis.

Minor :

1. Lytic bone lesions
2. Marrow plasmacytosis 10-30%
3. Monoclonal globulin spikes present in lower level
Normal IgM, IgA, or IgG.

Cytogenetic abnormalities:

1. Deletion of 13q
 2. Translocations involving Ig heavy chain locus on chromosome 14 like t (14:4), t(14:1), (14:6), (14:16)
- M/c sites of lytic bone lesions are **vertebrae** 66% > ribs > skull > pelvis > femur.
Lytic lesions result in bone pain, pathological #, cord compression etc.
 - Bone pain is m/c symptom which involves back (spine), ribs, sternum
 - Infections: m/c pneumonia, pyelonephritis
 - **Lab/f : Anemia** is normocytic normochromic type, hyperuricemia, ↑ESR
Clotting abnormalities (1, 2, 5, 7, 8 factor) and **hyperviscosity** (less common)
 - MM is a/w **hypercalcemia** which leads to *metastatic calcification* in kidney.
Renal failure & amyloidosis may occur late in the course of d/s
 - M-component : usually d/to IgG (53%) kappa
 - Serum β₂ **microglobulin** is most important single powerful predictor for **prognosis**
 - *Poor prognostic factors* are ---High labeling index, ↑LDH, ↑thymidine kinase, λ - light chain have poor p/g

- Kidney --- **primary amyloidosis** (not secondary), renal tubular necrosis, tubular cast in urine

- **Patho/f :**

- *Flame cell* (cells with fiery red cytoplasm),
- *Mott cell* (multiple grapelike droplets),
- *Crystalline rods and Dutcher bodies*
- *Russel bodies & plasma cells are seen.*

- **Alkaline phosphatase level is normal**

- D/d includes *benign monoclonal gammopathy* which have

<10% marrow plasma cell

<30gm/L of M-component

no Bence Jones protein in urine

no $\uparrow \text{Ca}^{++}$, no anemia

→ *Bence Jones protein is a monoclonal globulin (or immunoglobulin of light chain), found in blood or urine of 2/3 rd MM patients, mostly derived from MEU chains*

→ *Lymphoplasmacytoid lymphoma is the tissue manifestation of Waldenström's macroglobulinemia. Patients often have \uparrow IgM proteins*

Waldenström macroglobulinemia (WM)

- Involves bone marrow but **does NOT** cause lytic bony lesions, pathological #, **hypercalcemia**, renal d/s
- 20% excrete light chain **IgM kappa** (*characteristic IgM spikes*)
- **CI/F ---**
 - **A/w Lymphadenopathy & hepatosplenomegaly** (which is not seen in MM)
 - Hyperviscosity syndrome
 - Epistaxis, visual disturbance
 - CNS symptoms (like transient paresis, peripheral neuropathy, headache much more common than MM)

Lymphoplasmacytic Lymphoma

- Tissue manifestation of WM
- A/w chronic **hepatitis C**
- Tumour cells are **CD5 +ve**
- Patient often have monoclonal IgM protein.

BLOOD TRANSFUSION

Erythropoiesis sites (Fetal)

	Main site	Other sites
◦ Upto 6 week (6-8 week)	YS (mesoblastic phase)	
◦ 6-12 week	Liver	Yes
◦ 12-24 week	Liver, spleen	BM
◦ >24 week	BM (myeloid phase)	Liver

→ *Viruses causing suppression of erythropoiesis : Parvo-B 19 (most common) Hepatitis (non A, non B, non C), EBV, CMV, HIV.*

→ *Fetal erythrocytes have a short life span, which progressively lengthens to 90 d at term.*

→ *Hemoglobin content of fetal blood rises to the level of 12g/dl at midpregnancy, and at term it is about 18 g/dL.*

Life-span and t_{1/2} of---

Blood components	Life span	Half life
◦ Normal RBCs	◦ 120 days	60 days
◦ Fetal/neonatal RBC's	◦ 90 days	
◦ Platelets	◦ 7-12 days	2-3 days
◦ Transfused platelets	◦ 36 hours (1-7 days)	1 day
◦ PMNs	◦ 6-8	

D/s transmitted by BT/ blood products

- **Viruses**

- HCV (non-A non-B hepatitis), HBV (serum hepatitis), HAV, HGV, CMV
- HIV, HTLV I, II
- Parvovirus B-19
- West Nile virus

- **Bacteria**

Red cells and platelets are source of infection. Because most bacteria do not grow well at cold temperature, packed RBCS & FFP are not common sources of bacterial contamination. Exceptions are :

- *Yersinia, Pseudomonas --- can grow at 1-60C*
- *Coagulase negative staphylococci --- c/b transmitted by platelet concentrates*
- *Syphilis --- by fresh blood only*
- *Brucellosis*

- **Parasites**

- *Plasmodium (malaria)*
- *Trypanosoma cruzi (Chaga's d/s)*

• **Tickborne infections**

- Babesia
- Rickettsia rickettsii,
- Colorado tick fever

• **Prion d/s**

- CJDs

→ M/c infection transmitted by BT is --- CMV

→ M/c cause of post transfusion hepatitis --- HCV

→ M/c bacteria contaminating packed cell --- *Yersinia enterocolitica*

→ For patient receiving plasma products manufactured from pooled human blood (eg. Cryoprecipitate, FFP, clotting factors) risk of transmission of HCV, HBV, HIV is higher (20-30%).

→ While for those receiving albumin, immunoglobulins, HB Vaccine (heated at 60°C/ cold fractionated) risk is nil.

→ Acc/to national blood safety program mandatory tests before BT include : For HIV, HBV, HCV, malaria and syphilis

→ HEV is **not** known to be transmitted by BT

Blood Transfusion (BT)

- Normal blood volume is ~ 80 ml/kg in children, 70 ml/kg in adult male and 60 ml/kg in adult females. Blood volume in healthy adult is 5-6 L.
- Whole blood required for transfusion is 20 ml/kg. Blood products (FFP, PCV, platelets) are given 10-15ml/kg.
- Platelets preferably should be stored at room temperature (>24°C)
- Among blood components highest rate of infection seen with - Platelet concentrates
- Febrile non hemolytic reaction is the m/c reaction seen after BT.
- 10 mL/kg transfusion of blood in children in severe anemia raises the Hb level by ~ 2.5 gm%.
- M/c cause of coagulopathy in massive blood transfusion is --- Dilutional thrombocytopenia

Changes in stored blood

In RBCs	In plasma	Others
Progressive ↓ of intracellular ATP, K ⁺ & 2, 3 DPG (left shift of ODC).	↑ K ⁺ & NH ₃ ↑ Citrate & lactate ↑ Labile clotting factor (esp V & VIII)	Thrombocytopenia Micro aggregates formation

- Red cell survival is related to cellular level of ATP. The addition of adenine, a newer preservative (CPD-A), is preferred as blood can be stored for 35 days
- Old blood transfusion may lead to--- Hyperphosphatemia.

Massive Blood Transfusion

- Defined as either 5000 ml blood (whole blood) is transfused in < 24 hr or A single transfusion of >2500 mL
- Massive transfusion of blood causes - Hypothermia, hypocalcemia, hyperkalemia, metabolic acidosis, hypomagnesemia
- Hemosiderosis is related to repeated transfusion of blood or frequent blood transfusions
- Test done on non mismatched blood transfusion reaction --- Direct Coomb's test.

Clotting Factors

- 1 = Fibrinogen
- 2 = Prothrombin
- 3 = Thromboplastin
- 4 = Calcium
- 5 = Proaccelerin/ labile factor 6 = Nil
- 7 = Proconvertin
- 8 = AHF
- 9 = Christmas factor
- 10 = Stuart power factor
- 11 = Plasma thromboplastin antecedent, antihemophilic factor C
- 12 = Hageman factor, glass contact factor
- 13 = Laki Lorand factor

[Mnemonic: Fir Pappu to ealeutta pahucha nahi 1,2,3,4,5,6 Praying at christmas, Stuart planned hindu ladki 7,8,9,10,11,12]

- Factor VII is exclusive to the extrinsic system and hence it is not consumed in the clotting system
- Among the coagulation factors, factor XII deficiency does not produce bleeding, but thrombosis.
- vWF is present in platelets, endothelial cells & in plasma along with factor 8
- Cryoprecipitate contains -- Factor 8 + vWF multimer + fibrinogen + fibronectin + factor 13
- FFP contains -- Factor 8 & 9
- Adsorbed plasma contains -- Factor 5, 8, 11, 12
- Normal serum contains -- Factor 9, 10, 11, 12

BLOOD COMPONENTS THERAPY

	PCV (Red blood cells)	FFP	Cryoprecipitate	Platelet concentrates (PC)
Description	Whole blood – plasma	Plasma frozen within 8 hours of donation contain at least 0–70 U/ml of factor VIII	Precipitate formed when FFP is thawed at 4°C	
Storage	1–6°C	–18°C or less for 1 yr	–18°C or less for 1 yr.	Only blood product which c/b stored at room temp. at 20–24°C for days)
Content	Hct 70%	All coagulation factor and plasma proteins Factor XIII (30%)	Factor VIII (80–100 U) Fibrinogen (100–200 mg) vWF (40–70%)	
Indications	Anemic pt in compensated CCF Surgical Pt.	<ul style="list-style-type: none"> - Coagulopathies a/w liver d/s - Reversal of Warfarin therapy - DIC - Massive transfusion - AT III deficiency - Isolated coagulation factor deficiency 		<ul style="list-style-type: none"> - Cong/acquired aplastic anemia - BM infiltration with leukemia - Myoablative chemotherapy - DHF - SLE
Others	1 unit of PCV raises Hb by 1.5 to 2 gm%	Each unit of FFP ↑ clotting factor by 3%	Prepared from multiple donors, risk of infection is high	1 unit of platelet ↑ the count by 10,000

- Therapeutic dose of FFP is 10–15 ml/kg
- Transfused platelets survive for 1–7 days
- Spontaneous bleeding occurs when platelet count falls < 20,000
- Platelet transfusion in DHF or ITP is indicated if platelet counts are < 10,000.

Compatible blood groups for transfusion

Patient	Whole blood	Packed red cells	FFP	Platelet	Cryoprecipitate
O	O	O	O	O > any	O
A	A or O	A or O	A or AB	A > AB	A
B	B or O	B or O	B or AB	B > AB	A
AB	Any	Any	Any	AB	A

Blood Groups

- Blood group antigens are mucopolysaccharides. ABO antigens are found on red cells and most body fluids like saliva, semen, sweat (but NOT in CSF) or membranes of intestine, urothelium, vascular endothelium
- Commonest type of blood gp --- blood gp O
- ABO Incompatibility
 - Blood groups involved in ABO incompatibility --- O of mother & A, B or AB of baby.
[mnemonic to remember letter 'o' present in mother and a b in spelling of baby]
 - Blood required for exchange transfusion --- Group O packed RBCs (same Rh type as the baby's) with AB plasma
- Rh Incompatibility
 - Blood group involved in Rh Incompatibility --- Rh -ve mother, Rh+ve father, Rh+ve baby
 - Blood required for ET --- Group O packed RBCs Rh-ve with AB plasma

Compatible blood groups for patients

Patient	Whole blood	Packed red cells	FFP	Platelet	Cryo
O	O	O	O	O	O
A	A or O	A or O	A or AB	A > AB	A
B	B or O	B or O	B or AB	B > AB	A
AB	Any	Any	Any	AB	A

- For Platelet concentrate transfusion donor preferably has same ABO Rh group as recipient.
- M/c naturally occurring antibodies are --- Anti-Lewis IgM antibodies of no clinical significance
- Antigens located on platelets --- ABO, HLA, PL_{A1} (but Rh antigens are not present)
- In Erythroblastosis fetalis, antibodies are formed against antigen-D (anti-D are commonest), and also against some blood group antigens like C, E, Kell, Kidd, Duffy (but Anti-Lewis antibodies are usually not found)

IMMUNOPHENOTYPES & FLOW CYTOMETRY

Marker enzymes in leukemia/Lymphoma

Leukemia	Positive for	+ ve CD	- ve CD Markers
◦ AML	MPO +, Sudan black+ Chloroacetate esterase+		FA
◦ AML (Monocytic)	NSE+	13,33,34	
◦ AML (Erythroleukemia)	Glycophorin A+	-	
◦ AML (M ₇)	-	41, 61	
◦ ALL	PAS+		
◦ CLL (SLL)	Surface Ig	5,19,23	FMC7-
◦ HCL	TRAP+,FMC 7+	19,20, 25, 103	5, 23 -ve
◦ MCL (Mantle)	Surface Ig +ve for cyclin D1	5,19,20	23 -ve
◦ Follicular	Bcl 2,6 Surface Ig +ve, t (14:18)	10,19,20, 22	5
◦ Diffuse (DLBCL)		20,45	5,3
◦ Anaplastic LCL	EMA,Alk +	3,30	15,20
◦ Precursor B cell ALL	Tdt	19,10	
◦ Early Pre B cell ALL	Tdt + Cytoplasmic IgM heavy chain	19,10	
◦ Burkitt's	Surface Ig	10,19,20	34
◦ Follicular	Bcl 6	10,19,20,	5, Bcl 2 -ve
◦ Granulocytic sarcoma/ chloroma	MPO +, Lysozyme+		

◦ Hodgkin's (Classical) 15, 30

◦ Lymphocytic predominance type 20,45 15, 30

→ Follicular lymphoma has overexpression of BCL2 on chromosome 18,t (14:18)

→ CLL (SLL) is positive for both CD5 and CD 23

→ Mantle cell lymphoma (MCL) is CD 5 +ve but CD 23-ve, high levels of cyclin D1

→ HCL express pan B cell markers: Surface Ig usually Ig G, CD11c, CD25+CD 103 +, TRAP +ve but CD 23-ve

→ ALL with hypereosinophilic syndrome is char/by positive pre-B immunophenotypes (+ve TdT, CD10, 19, 20, 22) negative CD23, 5, 7 and myeloid markers MPO, CD33, 13. In PBS granular blasts present, very high peripheral blood eosinophilia. Common in male at 4 years age.

→ In eosinophilic leukemia --- eosinophilic blasts are found.

→ Plasma cell leukemia --- > 20% plasma cells in PBS, absolute plasma cell count $2 \times 10^9/l$.

→ Splenic lymphoma with villous lymphocytes --- +ve smIg CD 19, 20, 22, 796 FMC7.

→ CLL --- Immunophenotypes +ve CD 5, CD 19, CD 23 and -ve CD79, CD 22, FMC7. On histology there is diffuse proliferation of medium/ large lymphoid cells with high mitotic case, scanty cytoplasm and absent nucleoli.

→ Mesenchymal stem cells lack typical hematopoietic antigens namely --- CD3, CD14, CD15. Human MSC surface antigen profiles obtained by flow cytometry were positive for CD13, CD29, CD44, CD71, and negative for CD3, CD14, CD15, CD33, CD34, CD38, CD45, and HLA-DR.

HIGH YIELD POINTS

- Spur cell anemia is a feature of liver d/se, Laennec's cirrhosis.
- Hyposegmented neutrophils are seen in myelodysplasias.
- Hypersegmented neutrophils are seen in megaloblastic anemia
- Splenomegaly if found, reconsider the diagnosis of ITP, aplastic anemia
- Pyridoxine deficiency causes sideroblastic anemia.
- Commonest acute presentation of SCA is bone pain.
- Chloroma is a/w --- myelogenous leukemia.
- Low serum Haptoglobin is seen in --- newborn, hemolytic anemia, ineffective erythropoiesis, liver d/s, pregnancy, and estrogen therapy

- High serum Haptoglobin is seen in ---Chronic infection, malignancy, Hodgkin's d/s, active RA, SLE, biliary obstruction, OCP use, steroids use.
- New iron chelator useful in thalassemia (under trial) → Desferrioxime (ICL - 670)
- Splenic infarcts** are seen in --- Myeloproliferative d/s, Sick cell d/s, bacterial endocarditis.
- Osmotic Fragility of RBCs**
0.9% NaCl solution is isotonic with plasma
RBC begins to hemolyze in 0.48% → complete hemolysis 0.33%
- High OF in *Hereditary spherocytosis*
- Low OF in *Thalassemias*
- ABO antigens are NOT found in ---CSF
- NOT a complication of blood transfusion--- Leucocytosis
- NOT a cause of congenital hypercoagulability --- Antiphospholipid antibody syndrome.
- Splenomegaly is NOT common in --- Essential thrombocytosis
- NOT true of Mantle cell lymphoma --- CD 10 +ve
- NOT a B-cell marker --- CD 135
- NOT a cause of coomb's negative anemia --- SLE.
- Splenomegaly is NOT seen in --- Essential thrombocytosis/thrombocythemia
- NOT a congenital cause of hypercoagulable state--- lupus anticoagulant.

IMPORTANT / FREQUENTLY ASKEDNEGATIVE POINTS

- Thrombocytopenia does NOT occur in --- HSP**
- NOT a congenital disorder --- PNH
- NOT seen in PNH --- Massive splenomegaly
- Ferritin NOT found in --- Spleen.
- Dystrophic calcification is NOT seen in --- Multiple myeloma
- Alkaline phosphatase is NOT elevated in --- Multiple myeloma**
- NOT seen in multiple myeloma --- Hypocalcemia, normal ESR
- Iron overloading does NOT occur in --- PCV
- Reticulocytosis is NOT a feature of --- Anemia in CRF.
- Low retic counts are NOT seen in --- Hemolytic anemia.
- Leukoerythroblastic picture NOT seen in --- Thalassemia
- Red cell protoporphyrin is NOT increased in--- Thalassemia
- Raised ESR NOT is seen in --- Polycythemia vera, CCF, SCD, smoking
- Palpable purpura is NOT seen in --- Scurvy, ITP, DIC, TTP, thrombocytopenia.
- NOT seen in DIC --- Raised fibrinogen levels.
- Megaloblastic anemia is NOT seen in --- Cu deficiency
- NOT a common feature of Hodgkin's disease --- CNS involvement
- NOT included in international prognostic index of lymphoma --- Albumin and hemoglobin
- NOT true about histiocytosis --- Highly radiosensitive
- NOT a cause of coomb's negative anemia --- SLE

CLINICAL VIGNETTES

- A 8 year old child comes with complaints of subcutaneous bleed. Lab findings reveal his BT of 10 min, PT 15/13, APTT 32/26, & TT is 16/ 16. His platelet counts are normal. Most likely d/g is
- Hemophilia
 - Liver disease
 - Glanzman's thrombosthenia
 - Von Willibrand disease
- (Ans: C. Glanzman's thrombosthenia)

Approach to a child with bleeding

- Superficial (skin/ mucosal) bleed ---**
D/to Increased capillary fragility ---EDS, vasculitis, drugs
Look for platelets ---- if counts are low---Congenital/ acquired platelet defect
if counts are normal---functional defect
- Deep (joint/ muscular) bleed ---** Coagulation disorders
e.g. hemophilia, liver dysfunction

In Thrombosthenia --- Platelet counts may be normal or slightly reduced.

In Glanzman's thrombosthenia --- Platelet counts are normal . Platelet aggregation and clot retraction are absent

In Bernard Soulier d/s--- Platelet counts slightly reduced. Ristocetin induced agglutination defects

In Wiscott Aldrich

syndrome --- Platelets size is half of normal.

In Myeloid metaplasia

with myelofibrosis --- Giant platelets are seen

Q. A 62 year old male presents with generalised weakness. On examination there is moderate splenomegaly. PBS reveals pancytopenia. Most likely d/g is

- A. HCL
- B. CML
- C. Non-Hodgkins B-cell lymphoma
- D. Aplastic anemia

(Ans.: C. Non Hodgkins B- cell lymphoma)

Diagnostic Clue

HCL and CML are causes of massive splenomegaly
Aplastic anemia is char by---No hepatomegaly, no splenomegaly, no lymphadenopathy

Q. A 2 years old child presented with h/o ecchymotic spots off and on since birth. There is history of prolonged umbilical stump bleeding. He most likely has deficiency of:

- A. Factor IX
- B. Factor XIII
- C. GPIb
- D. Platelet

(Ans.: B. Factor XIII)

Q. A 25 years old female presents with Hb of 9 gm%, TLC $1200 / \text{mm}^3$, MCV 120 fL, and platelets 60,000. Most likely d/g is. [AIIMS May'2008]

- A. Myelofibrosis
- B. Aplastic anemia
- C. Megaloblastic anemia.
- D. PNH

(Ans. C. Megaloblastic anemia)

MCV is raised (> 100 fL). TLC and platelets may be decreased in megaloblastic anemia

Q. A 48 year old woman was admitted with a history of weakness for two months. On examination, cervical lymph nodes were found enlarged and spleen was palpable 2 cm below the costal margin. Her hemoglobin was 10.5 g/dl, platelet count $237 \times 10^9/\text{L}$ and total leukocyte count $40 \times 10^9/\text{L}$, which included 80% mature lymphoid cells with coarse clumped chromatin. Bone marrow revealed a nodular lymphoid infiltrate. The peripheral blood lymphoid cells were positive for CD 19, CD5, CD20 and CD23 and were negative for CD79B and FMC-7. What is the most likely diagnosis? [AIIMS Nov'05]

A. T- cell rich B-cell lymphoma with leukemic spillover in blood.

B. Chronic lymphocytic leukemia.

C. Mantle cell lymphoma.

D. A definite diagnosis cannot be made in this patient without lymph node biopsy.

(Ans: B. Chronic lymphocytic leukemia.)

Q. A 15 year-old boy presented with one day history of bleeding gums, subconjunctival bleed and purpuric rash. Investigations revealed the following results:

Hb, 6.4 gm/dL; TLC-26,500/mm³; Platelet-35,000/mm³; prothrombin time-20 sec with a control of 18sec; partialthromboplastin time-50 sec and Fibrinogen 10 mg/dL. Peripheral smear was suggestive of acute myeloblastic leukemia. Which of the following is the most likely?

[AIIMS May'06]

A. Myeloblastic leukemia without maturation.

B. Myeloblastic leukemia with maturation.

C. Promyelocytic leukemia.

D. Myelomonocytic leukemia.

(Ans.: C. Promyelocytic leukemia.)

Bleeding gums, subconjunctival bleed and purpuric rashes in this leukemic child are bec/ of development of DIC as suggested by thrombocytopenia \uparrow PT, \uparrow APTT with hypofibrinogenemia.

DIC is most commonly seen in acute promyelocytic leukemia (M3)

Q. A 17 years old boy presented with TLC of $138 \times 10^9/\text{L}$ with 80% blasts on the peripheral smear. Chest X-ray demonstrated a large mediastinal mass. Immunophenotyping of this patient's blasts would most likely demonstrate:

[AIIMS May'06]

A. No surface antigens (null phenotype).

B. An immature T cell phenotype (Tdt/CD34/CD7 positive).

C. Myeloid markers, such as CD13 Cd33 and CD15.

D. B cell markers, such as CD19 CD20 & CD22.

[Ans.: B. An immature T cell phenotype (Tdt/CD34/CD7 positive)]

The boy in the question is most likely suffering from ALL. Clues are

• $\text{TLC} = 138 \times 10^9/\text{L} = 138 \times 10^3/\mu\text{L} = 1.38 \text{ Lakh } \mu\text{L}$ and blast cells more than 80% are suggestive of leukemia/lymphoma

• Age group of ALL.

• When ALL presents as anterior mediastinal mass. It is most likely immature T cell phenotype so the most likely

answer is B.

- ❑ A patient presents with a platelet count of $700 \times 10^9/L$ with abnormalities in size, shape and granularity of platelets. WBC count of $12 \times 10^9/L$, hemoglobin of 11g/dl and the absence of the Philadelphia chromosome. The most likely diagnosis would be: [AIIMS May'06]

A. Polycythemia vera.
B. Essential thrombocythemia.
C. Chronic myeloid leukemia.
D. Leukemoid reaction.

[Ans. B. Essential thrombocythemia.]

As there is absence of Philadelphia chromosome CML is excluded. Now d/d of remaining 3 options

	Platelets	TLC	Hb
PV	↑↑	↑	N or ↑
Essential thrombocythemia	↑↑↑	N or ↑	N, ↓ O
Leukemoid reaction	N or ↑	↑	↓

- ❑ An elderly patient presents with generalised weakness and multiple punched out lesions in the skull radiograph. Which of the following investigation is best for diagnosis? [AIPGMEE' 09]

A. Serum electrophoresis
B. Serum calcium levels
C. Serum alkaline phosphatase
D. Bone scan

(Ans. D. Bone scan)

Multiple punched out lesions in skull vault are characteristic of multiple myeloma.

- ❑ A 70-years old male has a pathologic fracture of femur. The lesion appears lytic on X-ray film with a circumscribed punched out appearance. The curetting from fracture site is most likely to show which of the following?

[AIIMS May' 06]

A. Diminished and thinned trabecular bone fragments secondary to osteopenia.
B. Sheets of atypical plasma cells.
C. Metastatic prostatic adenocarcinoma.
D. Malignant cells forming osteoid bone.

(Ans. B. Sheets of atypical plasma cells.)

Elderly male in question is most likely suffering from multiple myeloma.

Points in favour are:

- Age – elderly
- Sex – male
- Pathological # are common
- Lytic punched out lesion on x-ray which is characteristic

- ❑ A patient presents with Hb 6 gm%, TLC 2000, has a normal DLC except for having 6% blasts; platelets are reduced to 80,000. There is moderate splenomegaly and lymphadenopathy on examination. The most likely diagnosis is [AIPGMEE' 01]

A. Leukemia B. Aplastic anemia
C. Hemolytic anemia. D. ITP

(Ans. A. Leukemia)

Hemolytic anemia is ruled out easily as there is no evidence of hemolysis.

- Pancytopenia and 6% blasts in PBS indicate a d/g of-- leukemia (aleukemic)
- Acute leukemias are a/w very high TLC, blasts > 30%
- Chronic leukemias are a/w variable TLC (acc to phases) and blasts < 30%
- In ITP --- Splenomegaly is uncommon
- In Aplastic anemia --- There is no splenomegaly, no lymphadenopathy, no hepatomegaly

- ❑ A 25 years old female presents with Hb of 8 gm%, TLC 8000 /mm³, MCV 55 fL with no history of blood transfusion in the past. Most likely d/g is [AIIMS May'08]

A. Beta thalassemia major
B. Beta thalassemia minor
C. Megaloblastic anemia.
D. Iron deficiency anemia

(Ans. D. Iron deficiency anemia)

- MCV is reduced and TLC is normal in the qn. Both of these points favour a d/g of IDA
- H/o BT is common in beta thalassemia major (Hb levels < 5gm%)
- H/o BT is uncommon in beta thalassemia minor or trait (but Hb levels are usually 10-12 gm%)
- H/o BT is occasional in beta thalassemia intermedia (Hb levels are usually in range of 5-10 gm%)

- ❑ A 13 years girl presents with fatigue. Laboratory investigations reveal Hb of 6.5 gm%, MCV 70 fL, MCH 22/ RDW 28.0/e there is no organomegaly but severe pallor is there. Most likely d/g is. [AIPGMEE' 10]

A. Beta thalassemia major
B. G6PD deficiency

C. Sideroblastic anemia.

D. Iron deficiency anemia

(Ans. D. Iron deficiency anemia)

Girl in qn have significantly ↓ Hb%, slight ↓ MCV, ↓ MCH suggesting microcytic hypochromic anemia most likely d/to IDA. Further RDW > 20 goes in favor of IDA. See table in hemato section

- Q A 9 year old girl bleeds excessively after tonsillectomy. Her investigation reveals a normal platelet count, and normal prothrombin time but increased APTT. What is the most likely cause. [AIPGMEE' 09]9]

A. Hemophilia A

B. Hemophilia B (factor IX deficiency)

C. Von Willebrand's disease

D. Factor V deficiency

(Ans. : C. Von Willebrand's disease)

- Hemophilia A or B are unlikely because they are X-linked recessive disorder and manifest in boys
- PT is prolonged in liver d/s, vitamin K deficiency and factor V deficiency
- **Von Willebrand's d/s (VWD)** is the m/c hereditary bleeding disorder. More common in females. It is an AD/AR condition. Deficiency results in manifestations of both platelet adhesion/ aggregation defect (bleeding from venules and capillaries e.g. post operative hemorrhage, epistaxis, menorrhagia, g.i. bleeding) and coagulation defect (echymoses, hemarthroses, post traumatic hematoma etc.) In this BT, APTT, and platelet aggregation are prolonged.

- Q A 6 year old boy presents with hemarthrosis of right knee. He had several episodes earlier and had a history of prolonged bleeding after trivial trauma. His maternal uncle had similar illness. O/e His growth and development is normal except for swelling and effusion in right knee. Her investigation reveals a normal platelet count, and normal prothrombin time but APTT is 110 sec. What is the most likely cause. [AIPGMEE' 09]

A. Hemophilia A

B. Hemophilia B (factor IX deficiency)

C. Von Willebrand's disease

D. Factor V deficiency

(Ans. : A. Hemophilia A)

- **Classic hemophilia** or hemophilia A manifests in boys with deep bleeding into joints/ tissues (hemarthroses) Bleeding may manifest at any age e.g. in newborn umbilical cord bleeding, prolonged bleeding after sports

injury, during tooth extraction, or circumcision.

- **Parahemophilia** or Owren's d/s is d/to deficiency of factor V. It is an AR condition and occurs in both gender.

- Q A 60 year old female with h/o 8 BT in last 2 years. Her investigation reveal : Hb 60 g/L, TLC - 5800, platelets - 3.4 lacks, MCV-60, RBCs 2.1 lakhs/ mm³. She is having hypochromic microcytic anemia. Which investigation is NOT required? [AIIMS Nov.'2010]

A. Evaluation for pulmonary hemosiderosis

B. Urinary hemosiderin

C. BM examination

D. GI endoscopy

(Ans. : B. Urinary hemosiderin)

- Q A 35 year old female presents with normal PT and prolonged aPTT. There was a past h/o cholecystectomy without any bleed 2 yrs back. What is the next Ix for clinical d/g. [AIIMS Nov '10]

A. Factor VIII assay

B. Anti-viper venom assay

C. Platelet aggregation test

D. Ristocetin cofactor assay

(Ans. : B. Anti-viper venom assay)

Asymptomatic patients without any bleeding during Sx and prolonged aPTT are likely to have lupus anticoagulant. Best test for diagnosis is Russel viper venom assay test.

In vWD activity of vWF is measured by ristocetin cofactor assay. 11.

- Q A Young male with AML was given induction therapy with cytarabine and idarubicin. However, persistent leukopenia was noted after this 6 weeks of the course of Induction therapy. What is the most likely cause? [AIPGMEE' 12]

A. Chemotherapy induced myelosuppression

B. Vitamin B12 Deficiency

C. Parvovirus infection

D. Persistent leukemia

(Ans. : A. Chemotherapy induced myelosuppression)

- Q Which of these is not a cause of increased MCV and normal MCH? [AIPGMEE' 12]

A. Aplastic anemia

B. Thalassemia

C. Vitamin B 12 deficiency

D. Hypoplastic marrow

(Ans. : B. Thalassemia)

Thalassemia is a cause of microcytic (not increased MCV) hypochromic anemia.

NOTES

Syndromes a/w Hemiplegia

Site of lesion	Syndrome	Same side (CN lesion)	Opposite side (Cont/L)	Additional / F
Midbrain	Weber's	3rd	Hemiplegia	
	Benedikt's	3rd	H	D/t lesion of red nucleus ataxia, static tremors
Pons	Millard- Gubler	7 (infranuclear)	H	± 6
	Raymond Foville's	7 (LMN type)	H	Paralysis of lat./conjug. gaze (ipsi/L)
Medulla	Schmidt's	9, 10, 11	H	
		Horner's synd	H	
Spinal cord	Brown Sequard	H + Post. column lesion	Pain & Temp. loss	[H = Hemiplegia]

- Paralysis of 3rd, 4th, 6th nerve with involvement of ophthalmic division of 5th cranial nerve is d/tto lesion of cavernous sinus.
- Nothnagle's syndrome is ipsi/L 3rd CN lesion + C/L cerebellar signs.
- Claude's syndrome combines the features of Nonthnagle's + Benedicts

- Intra-medullary tumours present like central cord syndrome, Dissociative anesthesia can be present.
- Presentation of extra medullary tumour depends upon size of the tumour and site from where compressing.
- AHC involvement causes wasting and weakness.

Spinal Cord Transection Syndromes

Syndrome	Seen in	C/F
Complete transection	-	UMN type at the site of lesion LMN type below site of lesion
Hemicord syndrome	Brown-Sequard	Pain and temperature lost on opp. side & vibration, fine touch and joint sense lost on same side
Posterior cord syndrome	Tabes dorsalis	Sensory ataxia, late bowel & bladder dysfunction
Postero lateral cord syndrome	SACD	
Central cord syndrome	Syringomyelia	Dissociate anesthesia (d/tto destruction of decussating fibres of STT), loss of pain and temp sense but preserved touch / pressure sensation, early bowel / bladder dysfunction
Anterior cord syndrome	Ant. spinal a. occlusion	-

Cauda equina syndrome

- Affects L3 to coccygeal nerve roots which form cauda equina.
- Causes are trauma to the lower back (collapse of vertebrae below L1), a midline disc herniation, or an intraspinal tumour (e.g. neurofibroma), congenital anomalies like meningomyelocele.
- C/I/f :
C/by paraparesis
 - LMN signs in legs with fasciculations and m/s atrophy
 - Loss of bladder functions and impotence are early signs
 - Loss of ankle and knee jerks
 - Sensory loss involves saddle area (sadal anaesthesia) as well as other lumbar and sacral dermatomes
- Sphincters are spared, hip flexion and sensation over anterolateral thigh are spared.

Conus medullaris syndrome

- Affects S3 to coccygeal segments which form cauda equina.
- Causes are trauma to the lower back (L1), prolapse L1/L2 intervertebral disc, or a small intramedullary tumour, posterior abdominal/ mediastinal surgeries.

- C/Lf: Characterized by neurological deficits which are b/L
 - Weakness of movements in feet
 - Paralytic bladder, fecal incontinence and impotence
 - Loss of achilles tendon reflex if S1 segment is involved
 - Sensory loss involves saddle area (**saddle anaesthesia**) in S₃ and Coccygeal dermatomes
- Injury to L4 - S2 segments, above the conus, results in **epiconus syndrome**. Which is c/by considerable motor disability of LL, **automatic reflex bladder** d/to sparing of sacral parasympathetic fibres.

Alport Syndrome

- Hematuria in a deaf and mute child.
- Triad of **hematuria + sensorineural deafness + ocular anomaly**.
- Recurrent episodes of gross hematuria occurring 1-2 days after an ARI episode are common. Earliest renal manifestation is asymptomatic microscopic hematuria, which may be intermittent in girls and younger boys
- Renal : hematuria, thinning and splitting of GBM, mild proteinuria, chronic glomerulosclerosis,
- M/c hereditary nephritis with X-linked-Dominant inheritance. 15% patients have AR inheritance, keratokonus
- B/L sensory neural deafness (which is never congenital).
- Ocular finding — anterior lenticonus.
- Mutations in COL4A5 gene with defect in type 4 (α5) collagen.
- Renal transplantation is usually necessary.
- Early lesions are detectable . Electron microscopy is diagnostic.

Note :

- M/c cause of gross hematuria in children is IgA nephropathy (Berger's disease).
- M/c cause of painless hematuria in an elderly is carcinoma bladder.

Angelman syndrome

- Happy puppet syndrome
- Intellectual and developmental disability
- Sleep disturbance, seizures,
- Jerky movements (especially hand-flapping)
- Frequent laughter or smiling, and usually a happy demeanor.
- Classic example of genomic imprinting: C/by deletion

or inactivation of genes on the maternally inherited chromosome 15.

Apert Syndrome

- Tower shaped head (Craniosynostosis)
- Syndactyly
- Cleft lip/ palate

Behçet's synd

- Relapsing iridocyclitis
- Recurrent genital & oral ulceration
- Pathergy test⁺
- Leukocytoclastic vasculitis

Bartter's synd (AR)

- Juxtaglomerular app. hyperplasia
- ↓ K⁺ d/to ↑ Renin & ↑ Aldosterone
- Hypotension despite hyperaldosteronism
- Metabolic alkalosis
- Nephrogenic DI
- Experimentally produced by Ang II-blocker
- AR inheritance
- Short stature

Budd chiari syndrome

- Thrombotic occlusion of hepatic veins
- C/F : Present few wks of delivery
- Triad : Sudden onset abdominal pain near term or shortly after delivery +
Tender hepatomegaly (most characteristics) +
Ascites → high protein content
- ALT / AST ↑, Jaundice

Caplan's Syndrome

Pulmonary nodule in a patient of pneumoconiosis

Carney Syndrome

- Gastric leiomyosarcomas.
- Pulmonary chondroma
- Extra adrenal paraganglioma

Churg Strauss Syndrome :

- Asthma
- Fever
- Eosinophilia

- Vasculitis
- Granuloma

Costen syndrome

- Involves temporomandibular joint d/to defective bite
- Otalgia, sense of blocked ears, tinnitus, sometimes vertigo

Dandy-Walker Synd

- Post fossa cyst & Hydrocephalus
- Defect of cerebellar vermis
- Obstruction of foramen of Magendie Luschka

Di-George Syndrome

- Isolated T-cell deficiency
- Thymic hypoplasia
- IgG & IgA response impaired
- Immunoglobulin concentration normal
- Abnormal ear, short philtrum, micrognathia hypertelorism
- Rx : Epithelial Thymic transplant

Down's Syndrome

- Also k/as 'Mangolism'
- Genetic basis
 - 95% d/to trisomy 21
 - d/to Meiotic non-dysjunction of maternal chromosome (derived from ovum)
 - 4% d/to Robertsonian translocation (Inherited)
 - 1% d/to Mitotic non dysjunction (Mosaics)
- ↑ Nuchal fold thickness (NFT) and ↓ femur length in a fetus by prenatal ultrasound is a reliable indicator of 21 trisomy. In USG fetus, Nuchal translucency/ thickening/ edema >5 mm at 14-18 weeks of gestation is characteristic of trisomy 21. Short femur and ↑ BPD/ FL ratio is also seen.
- Triple test in mother reveals ↑ MSAFP + ↑ β-hCG + ↓ UE. Dimeric inhibin A is used in quadruple test.
- M/c chromosomal anomaly. Incidence is 1 in 700
- Etio: In 85% of patients it is d/to meiotic non-dysjunction.
- Risk increases with advancing maternal age (in the age group 15-29 risk is 1:1500, in the age group 35-39 risk is 1:270, after 45 years risk is 1:50)
- Physical findings
 - Head:** Microcephaly, flat occiput, wide AF
 - Face:** flat nasal bridge,

Eyes: Upward slant (Mangoloid slant), Microcephaly, flat occiput, wide AF, Brushfield spots.

Ears: Low set ears

Chest: 11 pairs of ribs

Others: Hyperechoic bowel, thickening of cardiac papillary m/s in fetal ECHO, sanadal gap, clinodactyly

Note :

- *Mangoloid slant is seen in Down's, Lawrence Moon Beidl.*
- *Anti-mangoloid slant is seen in Apert, Treacher Collins, Cerebral gigantism, De George syndrome*

Durozzi's Syndrome

- Paraneoplastic syndrome a/w Erythrocytosis, polycythemia
- Hypertension
- Hypercalcemia
- ↑ ACTH (Cushing's), hCG, glucagon, prolactin, and Gn

Felty syndrome

- Thrombocytopenia
- RA
- Anemia
- Netuopenia
- Splenomegaly [Mnemonic : TRANS]

Foster Kennedy Syndrome

- Is optic atrophy with contra lateral papilloedema.
- A/w olfactory or sphenoidal meningioma.

Fanconi's Syndrome

- Also k/as De Toni Fanconi syndrome
- Aminoaciduria
- Phosphaturia (**Hypophosphatemic osteomalacia**)
- RTA (metabolic acidosis)
- Glycosuria

Foster Kennedy Syndrome (WRONG)

- A/w aortic insufficiency
- Concurrent urethritis
- Periosteal new bone formation
- Conjunctivitis

Foster Kennedy Syndrome

- Is optic atrophy with contralesional papilloedema.
- A/w olfactory or sphenoidal meningioma.

Fragile-X Syndrome

- Also k/as Martin -Bell or Escalante syndrome
- M/c inherited cause of mental retardation in males.
- FMRP protein deficiency.
- Females with F~ also show mental retardation.
- Fragile site is located on the long arm of X-chromosome (Xq27)
- Genetic defect is a large 2800 CGG trinucleotide repeat base pairs (up to 50 base pair repeats are normal)
- C/I/f includes
 - Long face, macrocephaly.
 - Prominent jaw
 - Large ears
 - Macroorchidism/ large testes
 - ADHD
- No increase risk of malignancy.
- Language delay is the m/c delay.

→ M/c genetic cause of MR is Down's syndrome .

→ M/c inherited cause of MR is Fragile -X syndrome .

Frey's syndrome

- Flushing & sweating of skin of parotid region during eating seen .
- after parotidectomy parasymp. nerve fibres supplying sweat glands of parotid area, are misdirected
- T/t → tympanic neurectomy (Jacobson's)

Gradenigo syndrome

- At petrous apex mastoiditis can produce
 - Pain,
 - Deafness
 - Ipsilateral Abducent nv. palsy

Gardener's S~

- Multiple osteomas
- Retractable Mesenteritis
- FAP

Heerfordt's

B/I parotid enlargement + ant.uveitis + 7th CN palsy . Fever may be present

Infantile tremor synd. (ITS)

- Self limiting d/s seen in 5 months - 3 years)
- Seen in exclusive breast fed infants.
- Almost exclusively in *males*
- Gradual mental & psychomotor retardation
- Pigmentary changes of hair & skin, pallor, tremor (usually generalized, coarse).
- Consciousness retained.
- C/c → subnormal intelligence.
- Lab/F → not pathognomonic
- Rx - Zn, Mg start weaning

Kallmann's syndrome

- AD disorder with maldevelopment of olfactory bulbs.
- Delayed puberty.
- Cong. anosmia usually in male
- Color blindness
- Cryptorchidism
- Hypogonadotropic Hypogonadism (↓ Gn, FSH & LH)
- Rx :- Pulsatile GnRH & androgen replacement

Kartagener syndrome

- Also k/as primary ciliary dyskinesia, or immature cilia syndrome or *Immotile cilia syndrome*
- Rare AR disorder d/to defect in ciliary lining of respiratory tract, sinuses, middle ear and fallopian tube.
- Triad of bronchiectasis + sinusitis + situs inversus.
- Dynein arm deficiency
 - nce of radial spokes/ -nce of central microtubules.
- Infertility is common d/to immotile sperms, defective ciliary action in FT.

Klinefelter syndrome : (47, XXY)

- Tall male with hypogonadism
- Mild mental retardation
- **Hyalinosis of seminiferous tubules** → Azoospermia
- ↑ FSH, LH & serum estradiol
↓ Testosterone
(M/c cause of hypergonadotropic hypogonadism)
- Gynecomastia
- ↑ risk of osteoporosis, emphysema, DM

Klippel-Feil synd

- Short webbed neck (fused cervical vertebrae)
- A/w hemivertebrae/Sprengel deformity.
- Stiff neck (limited neck movements)
- Low hair line

Laurence-Moon-Biedl (LMB) Synd.

- Mental Retardation.
- OBESITY
- Polydactyly/ syndactyly
- Retinitis pigmentosa
- Renal Anomalies
- Hypogonadism. [Mnemonic : MORPH]

Laron's syndrome

- ↑GH but CI/F of GH deficiency (Growth retardation)
- Low somatomedin
- Loren's dwarfism

Lowe's Syndrome

- Hypophosphatemic rickets
- Hypophosphatemic rickets
- Defect in CNS & eyes
- Aminoaciduria

Lofgren's

Joint symptoms + Erythema nodosum +B/L hilar lymphadenopathy

Lutembacher Syndrome

- ASD (Ostium secundum) + MS

Maffucci Syndrome

- Multiple enchondroma
- Hemangiomas
- Phlebolith

Marfan Syndrome

- Inherited as AD inheritance with nearly complete penetrance.
- Abnormal biosynthesis of **fibrillin-1** gene on chromosome 15q
- *Musculoskeletal*
Pectus carinatum or pectus excavatum
Arm span : height ratio > 1.05
US : LS ratio < 0.86 (adults), Positive wrist and thumb sign, protrusio acetabuli, pes planus
- CVS: Aortic root dilation (m/c) with or without AR, aortic dissection/ rupture, MVP
- Eyes: Ectopia lentis (lens upward and outward dislocated), megalocornea, RD.
CNS: Dural ectasia
- Other features: Face is long, extremities are thin and slender, skin is lax, hypotonia/ligament laxity, Arthrogryposis. males commonly affected.
- MVP develops early in life and progresses to MR in one fourth.
- Intelligence is normal.

Mc Cune Albright's Syndrome

(Polystotic fibrous dysplasia)

- Dysplasia of forehead /neck /buttock
- Precocious puberty.
- Cushing syndrome, acromegaly.
- B/L pheochromocytoma, ↑ T_4
- Spontaneous #, facial asymmetry
- Cafe au-lait spots.

Milk Alkali syndrome

- ↑ Serum Ca, PO_4
- Cr, BUN, HCO_3^- level
- Renal calcinosis
- Progressive renal failure
- **Hypercalcemia**

Mixed Gonadal dysgenesis

- Normal uterus
- 1° amenorrhoea
- No breast
- Ext. genitalia masculinized

Metabolic Syndrome

Any 3 of the following risk factor provide criteria for d/g of this syndrome-

- Abdominal obesity (Waist circumference > 102 cm in men & > 88 cm in women)
- TG level > 150 mg%
- Low HDL cholesterol (<40 mg% in males and <50 mg% in females)
- BP ≥ 130/85
- FBS > 110 mg%

Nail patella Syndrome

- AD disorder
- Nails are small (30-50% size), atrophied .
- Also known as hereditary osteo-onychodysplasia (HOOD).
- Small patella leading to unstability of knee joint.
- The white crescent shaped area located at the base of fingernails and toenails is k/as lunula. The lunula is triangular in NPS.
- Iliac horns.

NAME Syndrome

- Nevi
- Atrial myxoma
- Myxoid neurofibroma
- Ephelids

NARP Syndrome

- NARP syndrome is a maternally inherited **mitochondrial** disorder a/w mutation in the mtDNA gene MTATP6.
- C/by triad of Neuropathy (neurogenic m/s weakness) + Ataxia + Retinitis Pigmentosa (NARP)
- Begins in childhood or early adulthood
- Most people experience numbness, tingling, or pain in the arms and legs (sensory neuropathy), muscle weakness; and problems with balance and coordination (ataxia), vision loss caused by RP.
- NARP syndrome is d/to mutations in the MT-ATP6 gene.
- Changes are seen in mitochondrial DNA.

Nelson Syndrome

Pituitary tumour developing following b/L adrenalectomy

Noonan's syndrome

- Normal karyotype & gonads
- *Subnormal intelligence*
- Short stature, webbed neck
- Antimongoloid slant
- Pulmonary stenosis, HOCM
- Cubitus valgus
- Ptosis

Osler-Rendu - Weber Syndrome

- Spider like hereditary hemorrhagic telangiectasias (on face, lips, ear, forearm)
- Recurrent epistaxis & G.I. bleeding
- A-V malformations
- Maculopapular lesions on face, palm, mm
- Cirrhosis, clubbing, cyanosis
- AD inheritance.

Patau Syndrome ($M^3 C^5- P$)

- Mental & Growth Retardation (Severe)
- Microphthalmia, Microcephaly
- Capillary Hemangioma
- Coloboma of iris, Cataract, Cleft palate
- CHD (VSD, ASD, PDA)

Pierre - Robin Syndrome

- Hearing defect
- Mandibular hypoplasia
- Cleft palate
- Respiratory distress
- Ptosis, RD, Cong. Glaucoma
- Mental retardation.
- Micrognathia
- Glossoptosis

POEMS Syndrome

- Polyneuropathy (peripheral nerve damage)
- Organomegaly
- Endocrinopathy
- Edema
- M-protein (Multiple myeloma)
- Hyperpigmentation and hypertrichosis

Prader Willi syndrome

- Obese child with severe hypotonia & areflexia
- Feeding problem at birth
- Hyperphagia → OBESITY (6 mth - 2 yr)
- Short stature
- Hypogonadotropic hypogonadism
- Loss of paternally inherited genes on **chromosome 15** and maternal imprinting

Prune Belly (Eagle- Barret) Syndrome

- Triad of:
Abdominal m/s deficiency +
Cryptorchidism +
Urinary tract abnormalities
- Also k/as Eagle -Barret syndrome

Reiter's Syndrome

- Also k/as Leroy syndrome or Friesseger -Leroy syndrome.
- Concurrent urethritis
- Periosteal new bone formation
- Conjunctivitis
- Polyarthritis (UP CA-R)

Sweet Synd

- F > M.
- *Yersinia* infection
- Red-papular rash
- Neutrophilia
- Acute non lymphocytic leukemia
- Fever

Swyer Syndrome

- Pure Gonadal dysgenesis
- X Y Karyotype
- Normal uterus
- 1° amenorrhoea
- Streak Gonds
- Normal female int. & ext. genitalia

Turner syndrome

- Monosomy X or 45, XO : Female phenotype (XO Karotype)
- Underdeveloped uterus
- Under developed breast

- 1° amenorrhoea , m/c *cause of primary amenorrhea*
- Intelligence normal
- Short stature, webbed neck
- Widely placed nipples, shield breast
- Peripheral lymphadenopathy.
- Associated with
 - horse shoe kidney
 - cystic hygroma
 - coarctation of aorta
 - Lymph edema of dorsum of hands/feet's
- Short 4th MC, MT
- Chromosomal mosaicism (45X/46XX)

Treacher Collin's syndrome

- Mandibulofacial dysostosis
- hypoplasia of zygomatic bone & -nt its arch
- coloboma of lower eyelid
- ears are malformed (low set, pegs, pits)
- Hypoplasia of Malleus/incus
- Anti - Mangoloid slant
- AD inheritance

Vogt. Koyanagi Harada Syndrome

- B/L anterior uveitis
- Vitiligo, tinnitus, hearing loss
- Aseptic meningitis
- Hypopigmentation (esp. over face and scalp)

Wallenberg syndrome

- d/to thrombosis of PICA causing ischemia of lat. part of medulla, so called Lateral medullary synd.
- char/ by—Horner's synd. + dysphasia, dysphonia, vertigo, ataxia, loss of pain & temp. sense on ipsi/L face + Cont/ L limbs.

Waardenbrug Syndrome

- White forelock of hair
- Heterochromia iridis
- Depigmentation of skin
- Deafness (u/L or b/L SNHL)

Wiskott - Aldrich Synd

- X-linked R
(functional disorder of platelet with thrombocytopenia)
- Dermatitis, immuno deficiency, hemorrhagic diathesis

- Platelet : size half, ↓ α -granules
- Boys are anergic (abnormal sialoporia).
- ↓ IgM, IgE ↑ & IgA, IgG = N
(remember M minus & E elevated)

Wolf Ram Synd. (DIDMOAD)

- DI
- DM
- Optic Atrophy
- Deafness

Restless Leg Syndrome

M/c cause is iron deficiency anemia. Other causes are uremia, pregnancy, sleep apnea, varicose veins, folate deficiency, Other conditions a/w RLS are thyroid disorders, parkinsonism, Sjogren's syndrome, RA, coeliac d/s etc.

Schmidt's Syndrome

PGA-II which presents in adults with thyroiditis, adrenal insufficiency & DM-1

Sick Sinus Syndrome

- Sinus pauses > 3 seconds and syncopal episodes

Soto Syndrome

- Cerebral gigantism
- Autism
- Hypotonia
- LGA baby (Macrosomia)
- NSD-1 gene mutation

Stauffer Syndrome

- Hepatic dysfunction without liver metastasis
- Hepatomegaly
- ↑ PT, APTT, ALP, S. haptoglobin
- ↓ K⁺ d/to ↑ Renin & ↑ Aldo

Steel Richardson Syndrome

Progressive supranuclear palsy, pseudobulbar palsy, frequent falls (gait disturbances), Parkinsonism
Dementia, difficult swallowing, difficulty in moving the eye vertically, constipation, urinary incontinence

Stoke - Adams Morgagni Syndrome

- Also k/as stokes - Adams attacks
- Syncopal attacks d/to high degree AV block (prolonged PR interval, BBB)
- Arrhythmia are often transitory

Sudden Infant Death Syndrome (SIDS)

- Males are affected more than female.
- Highest risk at 2-4 month of age, with most deaths by 6 months.
- Autopsy findings are NOT pathognomonic.
- Risk factors –

Family history	Smoking in mother
Prematurity	Cocaine abuse
Metabolic (fatty acid deficiencies)	Low SES, increase parity
Prolonged QT syndrome	Prone sleep position of infant

→ Evidences suggest that deficiency of fatty acid synthesis is implicated in SIDS.

→ Parental smoking is most important risk factor.

Tumour lysis syndrome

- Seen in t/t of Burkitt's lymphoma, ALL
- Characterized by -
 - Hyperkalemia
 - Hyperuricemia
 - Hyperphosphatemia
 - Lactic acidosis
 - Hypocalcemia (All increased except Ca⁺⁺)

Absent radius is seen in

- TAR syndrome
- Holt oram syndrome
- Fanconi anemia
- VATER syndrome
- Trisomy 18 (Edward syndrome)

SOME IMPT. NEGATIVE POINTS

- NOT seen in a patient of Down syndrome.--- Undescended testis
- NOT seen in VHL (Von Hippel- Landau) syndrome --- Gastric cancers

- Nerve NOT involved in entrapment syndrome --- Femoral nerve
- NOT seen in Klippel- Feil syndrome --- Elevated scapula
- NOT a cause of Carpal tunnel syndrome --- Addison's d/s
- NOT true about Eaton- Lambert syndrome --- Decremental response to repeated stimuli

CLINICAL VIGNETTES

1. A young, tall, thin male with arachnodactyly has ectopia lentis in both eyes. The most likely diagnosis is:

[AIIMS Nov'05]

- A. Marfan's Syndrome B. Marchesani Syndrome
C. Homocystinuria D. Ehlers Danlos syndrome

(Ans. A. Marfan's Syndrome)

2. A 25 yr old male presents with renal failure. His uncle died of renal failure 3 yrs ago. On slit lamp examination, keratokonus is present. The most likely diagnosis is:

[AIIMS Nov'10]

- A. Autosomal dominant polycystic kidney d/s
B. Autosomal dominant polycystic kidney d/s
C. Alport syndrome
D. Denys- Drash syndrome

(Ans. C. Alport syndrome)

Alport syndrome is an AD condition a/w renal failure, anterior lenticonus.

Danys-Drash syndrome is an AD condition a/w mutations in WT1 gene and c/by diffuse mesangial sclerosis, genitourinary tumours and pseudohermaphroditism.

3. A patient presents with malena, hyperpigmentation over lips, oral mucosa and skin; and his sister is also having similar complaints. The diagnosis is: [AIPGMEE' 2000]

- A. Peutz Jegher's Syndrome
B. Familial Adenomatous Polyposis
C. Gardner's Syndrome
D. Villous Adenoma

(Ans: Peutz Jegher's Syndrome)

4. After a leisure travel a patient came with gritty pain in the eyes and joint pains. The most probable diagnosis is:

[AIPGMEE' 2000]

- A. Reiter's Syndrome B. Behcet syndrome

- C. Sarcoidosis D. SLE

(Ans: A. Reiter's Syndrome)

Gritty sensation in eyes c/b d/to conjunctivitis

Reiter's Syndrome

Reactive arthritis c/by acute arthritis + conjunctivitis + rashes. A/w HLA B 27

Behcet's Syndrome

C/by mouth ulcers (herpetiform) + vasculitis + severe iridocyclitis

Sarcoidosis

C/by lung involvement + iridocyclitis + lacrimal gland enlargement + LN granuloma

SLE

C/by Iritis/episcleritis + rash + Raynaud's phenomena

NOTES

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* HEMANGIOMAS Associated Syndromes

① PHACES

② CORTMAN:
Cutaneous Hemangiomas +
MASSIVE OSTEOCLASTS

③ Bannayan-Riley-Ruvulosa:
MACROcephaly
Lipomas
Hemangiomas - AD

1. Constrictions of esophagus : CALD

Constrict	At Level of	Distance from incisor teeth	
		In Adult (x)	In Children (x-1) / 2
1st	Cricopharynx (C6)	15 cm.	7 cm.
2nd	Arch of Aorta (T4)	25 cm.	12 cm.
3rd	Left Bronchus or Bifurcation of trachea (T5)	27 cm.	13 cm.
4th	Diaphragmatic opening (T10)	40 cm.	18 cm.

2. MeniGococci ferments : Maltose & Glucose
Gonococci ferments : Glucose only

3. Amide linked local Anesthetics

All Amide linked LA have -i- (do'nt consider -i- of caine)

Amide: Lido (caine)
 Bupiva (caine)
 Dibu (caine)
 Prilo (caine)
 Ropiva (caine)
 Mepiva (caine)

4. To remember action of all prostaglandins, leukotrienes and thromboxane A_2 -

Use **DALF**

D = $PG-D_2$
A = $Tx-A_2$
L = Leukotrienes
F = $PGF_2\alpha$

Bronchoconstrictor

D A L F

Vasoconstrictor

Among COX and LOX pathway derivatives

DALF are bronchoconstrictor

(rest are bronchodilator)

Only A, L are vasoconstrictor (rest are vasodilator)

(Bronchoconstrictor are PGD_2 , $Tx-A_2$, LT & $PGF_2\alpha$ & others PGE_1 , PGE_2 , PGI_2 are bronchodilator)

i.e. $PG-D_2$ is bronchoconstrictor + vasodilator

$Tx-A_2$, Leukotrienes - is broncho+ vasoconstrictor

$PGF_2\alpha$ - is bronchoconstrictor + vasodilator

So it is clear that inflammatory mediators like eg. prostaglandins, Bradykinin, histamine, prostacyclin all are vasodilators

5. Corticosteroids cause --- LEB low
 (Lymphopenia, eosinopenia, basopenia) but neutrophilia.

6. Dimorphic fungi (BimorPPHiCS)

Bi = Blastomycosis

mar P = Penicillium Marneffi

P = Paracoccidiomycosis

Hi = Histoplasmosis

C = Coccidiomycosis

S = Sporothrix

7. (I) Eggs of following parasite floats in saturated NaCl solution

HEAT **H** = H nana
E = Enterobius vermicularis
A = Ascaris (fertilized eggs)
T = T. Trichuria

(II) Which do not float :

SUIT **S** = Strongyloides larva
U = Unfertilized eggs of ascaris
I = Intestinal flukes
T = Taenia

8. Oviparous females in nematodes :

HEAT **H** = Hookworm
 (A. Duodenale & N. Americans)
E = Enterobius vermicularis
A = Ascaris
T = T. Trichiura

9. Auto infection is seen in :

Chhotu **SETH** **C** = Capillariasis
S = Strongyloides

E = Enterobius
T = Taenia solium
H = H. nana

10.(I) Parasites which migrate to lung/sputum examination is useful in :

SHAPE S = Strongyloides
H = Hookworms
A = Ascaris
P = Paragonimus
Westermani
E = Echinococcus

(if secondary Infection of lung occurs)

(II) Parasites which does not go to lung/absent in sputum:

WPW W = Whipworm
(Trichuris trichiura)
P = Pinworm (Enterobius)
W = Wucheria bancrofti

N.B. Wucheria bancrofti causes pulmonary eosinophilia but is not present in sputum (or does not go to lung).

11. Non-enveloped viruses :

PAP(DNA Viruses) PCR (RNA Viruses)
Parvo Adeno Papova Picorna Calci Rheo

12.(I) Segmented viruses = BORA

(II) Viruses with negative strand = BOPA

(III) Viruses with helical symmetry = BOCA

B = Bunya
O = Ortho-myxo
R = Reo,
P = Para-myxo,
C = Corona
A = Arena (Lasa fever virus)

13. Cranial accessory nerve supplies 3 'P' :

Palate
Pharynx
Palatoglossus

Mandibular nerve supplies 2 tensors: -

Tensor tympani
Tensor palati

N.B. :

1. All muscles of Palate are supplied by cranial accessory nerve except Tensor Palati (which is supplied by Mandibular nerve)

2. All muscles of Pharynx are supplied by cranial accessory nerve via vagus except Stylopharyngeus (which is supplied by 9th nerve)

3. All muscles of Tongue are supplied by Hypoglossal nerve except Palatoglossus (which is supplied by cranial accessory nerve).

4. All muscles of Larynx are supplied by recurrent Laryngeal nerve except Cricothyroid (which is supplied by External Laryngeal nerve)

5. All muscles of Face are supplied by Facial nerve except LPS (which is supplied by Oculomotor nerve)

14. Muscles supplied by musculocutaneous nerve:

BBC B = Biceps brachii
B = Brachialis
C = Coracobrachialis

15.(I) Branches of facial nerve in facial canal:

CSP C = Chorda Tympani
S = Stapedius
P = Petrosal

(II) Branches of facial nerve at exit at stylomastoid foramen:

DSP D = Digastric Branch
S = Styloid Branch
P = Posterior Auricular

16. Branches of subclavian artery :

Vit.C,D V = Vertebral artery (from 1st part)
i = Internal mammary artery
(Internal thoracic artery)
t = Thyrocervical trunk
C = Costocervical trunk
D = Dorsal Scapular artery

17. Branches of Basilar artery :

ALPS A = Anterior inferior cerebellar artery
L = Labyrinthine artery
P = Pontine artery
S = Superior cerebellar artery

18. Foramen present in Greater Wing of Sphenoid:

ROSE R = Rotundum
O = Ovale
S = Spinosum
E = Emissary (Sphenoidal)

19. Direction of nasolacrimal duct :

BLD (Bld for blood)

B = Backward
L = Laterally
D = Downward

20. Poisons detectable in bone :

TARA T = Thallium
A = Arsenic
R = Radium
A = Antimony

21. Uses of Danazol : [KDT - 304]

D-E FGHI-MP

D = Danazol
E = Endometriosis
F = Fibrocystic breast disease
G = Gynecomastia
H = Hereditary angioneurotic edema
I = Infertility
M = Menorrhagia
P = Precocious puberty in boys.

22. Uses of Colchicine :

BPLMAGIK

B = Behcet syndrome
P = Psoriasis
L = Liver cirrhosis
M = Mediterranean fever
A = Amyloidosis
G = Gout,
i = It is a inhibitor of mitosis
K = Kala-azar

23. Components of α -ketoglutarate dehydrogenase complex:

My TLC False Negative

M = Mg^{++}
T = TPP
L = Lipoic acid
C = CoA-SH
F = FAD
N = NAD^+

24. Blood flow to various organs : ml/min.

L	K	M	B	S	C
1500	1250	1000	750 (or 850)	500	250

L = Liver
M = Muscle
S = Skin
K = Kidney
B = Brain
C = Coronary (Heart)

25. Dose reduction in Renal failure not required in (Drugs safe in renal failure) :

DME N C₇R

D = Doxycycline
M = Mezlocillin & Metronidazole
E = Erythromycin
N = Nafcillin
C = Cephalexin
Cefaclor
Cefoprazone
Ceftriaxone
Chloramphenicol
Clindamycin
Carbenicillin
R = Rifampicin & Rifabutin

26. (I) Causes of Hypercholesterolemia :

MONA P-PCT

M = Myxedema (Hypothyroidism)
O = Obstructive liver disease
N = Nephrotic syndrome
A = Anorexia nervosa
P = Porphyria
P = Progestogens
C = Cyclosporine
T = Thiazides

(II) Causes of Hypertriglyceridemia :

PM CA Office DELHI Me S³ituated Tha

P = Pregnancy
M = Monoclonal gammopathy
C = CRF
A = Alcohol
O = Obesity
D = DM
E = Estrogen
L = Lymphomas & Lipodystrophy
H = Hepatitis (Acute)
I = Ileal bypass surgery
M = Multiple myeloma
S = SLE, Stress & Sepsis
Tha = Thiazides

(III) Causes of Hypocholesterolemia :

M³ALT

M = Malnutrition, Malabsorption
Myeloproliferative disease
A = AIDS

L = Liver disease (Chronic)

T = Tuberculosis

(IV) Causes of Low HDL :

MOCBA M = Malnutrition

O = Obesity

C = Cigarette smoking

B = Beta blockers

A = Anabolic steroids

27. LAP Score is low in :

CP **C** = CML

P = PNH

28. Risk of acute leukemia (ALL) increases in :

ABCDE **A** = Ataxia telangiectasia

B = Bloom's syndrome

C = Congenital hypogammaglobulinemia

D = Down's syndrome

E = EBV

29. Some interesting points about Japanese Encephalitis:

- * Case fatality rate **30%** average (actually 20-40%)
- * Immunity develops after **30** days of vaccination
- * Immunity persist for **3** years
- * Revaccination required after **3** years
- * Vaccination required for children <3 years
- * Insecticide spray required upto **3 Km.** range
- * Death occurs in J.E. in **3x3=9** days
- * Incubation period 7-15 days average **9 (3x3)** days

30.(I) Disease transmitted by Louse/ lice:

PERT **P** = Pediculosis

E = Epidemic typhus

R = Relapsing fever

T = Trench fever

(II) Disease transmitted by Rat-flea :

BEEnCH **B** = Bubonic plague

En = Endemic typhus

C = Chiggerosis

H = Hymenolepis diminuta

(III) Disease transmitted by Culex :

BJP **W**on in Centre

B = Bancroftian filariasis

J = JE

P = Polyarthritis (viral)

W = West Nile fever

C = Culex

(IV) Disease transmitted by Hard ticks :

ITBP Kc V²iR²

I = Indian Tick typhus

T = Tularemia

B = Babesiosis

P = Paralysis (tick)

K = KFD in India

Vi = Viral encephalitis

Viral Hemorrhagic
fever/Colorado fever

R = Rocky mountain spotted fever

Russian spring summer encephalitis

31.(I) Clotting factors which are vitamin-K dependent :

279/10 (279 for all out)

Cumulative Score

i.e. factor II, factor VII, factor IX, factor X, protein C & protein S are vitamin-K dependent.

(II) Clotting factors which are synthesized by liver :

279/10 C.S. + 15 runs extra

i.e. factor II, factor VII, factor IX, factor X, protein C, protein S, factor I & factor V are produced by liver.

(III) Cranial nerves which have parasympathetic fibres :

379/10 (379 for all out)

i.e. cranial nerves 3rd, 7th, 9th & 10th have parasympathetic out flow.

(IV) Normal serum contain factor 9,10,11,12.

(V) Adsorbed plasma contain factor 5,8,11,12

32. In Argyll Robertson's Pupil :

ARP $A \rightarrow R \rightarrow P$ = Accommodation

Reflex Present

$A \rightarrow R \rightarrow P$ = Pupillary (light)

Reflex Absent

33. Uses of D-penicillamine :

Use Pen & Start Writing MLC₃ In Rough

S = Scleroderma

W = Wilson's disease
 M = Mercury poisoning
 L = Lead poisoning
 C₃ = Copper poisoning,
 Cystinuria, Cystinosis
 I = Indian childhood cirrhosis
 R = RA

34. Uses of Dapsone

D-MRD

D = for Dapsone

M = Madura foot

R = Rhinosporidiosis,
 Resistant chloroquine malaria
 D = Dermatitis herpetiformis.

35. Arrangement of structures :-

At hilum of kidney	At femoral triangle	At intercostal groove
From anterior to posterior (VAP)	From medial to lateral (LVAN)	From above downwards (VAN)
- Renal v	- lymphatics, femoral vein	- Intercostal vein
- Renal a.	- Femoral artery	- Intercostal artery
- Renal pelvis	- Femoral nerve,	- Intercostal nerve

In Popliteal fossa	In upper part	AVN (Med. → lat.)
	In middle part	NVA (Superficial to Deep)
	In Lower part	NVA (Med. → lat.)

In Cubital fossa	Medial	MBBR
	→ lateral	(Median n., brachial a., biceps tendon, radial a.)

At the Porta hepatis DAV (ant. post.)	D = bile duct
	A = hepatic artery
	V = Portal vein

36. To remember various hemoglobinopathies :

Sickle Cell Disease Encounters / Very Low Growth Level

Hb-S = Valine in β⁶ for glutamic acidHb-C = Lysine β⁶ " " "Hb-D = Glutamine β¹²¹ " " "Hb-E = Lysine β¹² " " "

37. MRS DOP

MCP Joints are involved in RA

SLE

DIP Joints are involved in Osteoarthritis

Psoriasis

38. Mohmd Raffi sing slow & Piña zz Miss ani fast :

So slowly adapting touch receptors are

- Merkel's disk
- Ruffini's endings

Rapidly adapting touch receptors are

- Pacinian corpuscles
- Meissner's corpuscles

39. Diet avoided in celiac disease (Gluten sensitive enteropathy)

BROW

- Barley
- Rye
- Oat
- Wheat

40. Actions of Morphine [inhibits CTV]

C = Cough centre

T = Temperature centre

E = Causes emesis

V = VMC

41. Causes of ↑ sweat chloride

Chitrakar M.F. Hussain Madhuri Dixit G Par Fida Hai

C = Cystic fibrosis

M = Malnutrition

F = Familial cholestasis

H = Hypoparathyroidism

M = Mucopolysaccharidosis

D = Dysplasia ectodermal

G = G-6-Phosphatase Deficiency

P = Pancreatitis

F = Fucosidosis

H = Hereditary nephrogenic DI.

42. Corticosteroids causes LEB low

i.e. L = Lymphocytes

E = Eosinophils

B = Basophils

Lymphopenia because of lympholytic effect, but neutrophilia and leucocytosis

43. To remember all the OSTEO CHONDRITIS :

Calcutta Vali Sunder Radiologist Fatima Malik OT Se Chal

Ke Nikli Pahunchi Fir Panna College Ki Library

Calcutta / Vali

Calvé's ds = Vertebral body (central nucleus)

Sundar / Radiologist

Scheuermann's ds = Ring epiphysis of vertebrae

Fatima / Malik

Freiberg's ds = Metatarsal head

O / T

Osgood salter's ds = Tibial tubercle

Se / Chal

Sever's ds = Calcaneal tuberosity

Kar / Nikli

Köhler's ds = Navicular bone

Pahunchi / Fir

Perthe's ds = Femoral head

Panna / College

Panner's ds = Capitulum

Ki / Library

Kienböck's ds = Lunate bone

6 = Nil

7 = Proconvertin

8 = AHF

9 = Christmas factor

10 = Stuart power factor

11 = Plasma thromboplastin antecedent,
antihemophilic factor C

12 = Hageman factor, glass contact factor

13 = Laki Lorand factor

[Mnemonic : Fir Pappu to calcutta pahucha nahi

1,2,3,4,5,6

Praying at christmas, Stuart planned hindu ladki

7,8,9,10,11,12]

NOTES

44. Uses of Chloroquine

MEDAL

- Malaria
- Extra-intestinal (hepatic) amoebiasis
- DLE
- Leprosy reaction
- RA

45. Causes of renal papillary necrosis

ADIPOSE

- A = Analgesic nephropathy
- D = DM
- I = Infarct in shock
- P = Pyelonephritis
- O = Obstructive uropathy
- S = Sick cell nephropathy
- E = Ethanol

46. Psammoma bodies are found in P sa m (remember with the first four letters P sa m of Psammoma)

- P = Papillary carcinoma (of thyroid, of kidney/ RCC)
- sa = Serous cystadenoma
- m = Meningioma

47. CLOTTING FACTORS

- 1 = Fibrinogen
- 2 = Prothrombin
- 3 = Thromboplastin
- 4 = Calcium
- 5 = Proaccelerin/labile factor

IMPORTANT POINTS

- Passavant's ridge is d/ to palatopharyngeus.
- Epiglottis develops from 4th arch.
- Quadrigeminal artery supplies tectum of midbrain.
- Vasa vasorum is blood vessels plexus supplying blood vessels.
- Vaginal epithelium – stratified squamous non keratinized
- FT epithelium – ciliated columnar
- Tunica media is found in all blood vessels except veins.
- Venous sinuses are sub-fascial in location.
- Clavicle peculiarities - Only long bone which lies horizontally, 1st long bone to ossify, Ossifies from 2 primary centres. only long bone to ossify in membrane.
- Nutrient artery enters a long bone through **diaphysis** through an oblique canal & goes towards the growing ends.
- Cancellous/spongy bone are m/c affected by osteoporosis becoz they are more metabolically active than cortical bone.
- Blood supply of medial surface of cerebral hemisphere is by ACA.
- **Gallaudet fascia**: Deep fascia of perineum or its continuation.
- **Gallen's anastomosis** is connection b/w SLN (Superior laryngeal nerve) and ILN (Inferior laryngeal nerve).
- Froment sign is used for deep br. of ulnar nerve. Tests adductor pollicis m/s.
- Tractus solitarius is responsible for gustatory function.
- Multi unit smooth m/s is seen - Iris.
- Subpubic angle is 80°-100° in gynaecoid pelvis.
- Subscapularis attaches to upper end of humerus.
- Suture b/w bilateral parietal occipital bone - Lamboid suture.
- Long term memory is stored in neocortex.
- VPL of thalamus carries pain and temperature sensation.
- Largest vertebral body - in lumbar region.
- Length of trachea is 11 cm.
- Trachea b/s is by inferior thyroid artery.
- **The oblique fissure** T2-T3 vertebra to the level of 6th costochondral junction anteriorly.
- **The septomarginal trabeculae (moderator bands)** are seen in rt ventricular apex.
- **The deep cardiac plexus** is located in front of the bifurcation of trachea.
- Medullary cavity is absent in - sesamoid bone
- Arch of aorta starts at T4 level, reaches T3 and ends at T4. Corresponds to costal cartilages 2nd and 3rd.
- Esophagus pierces the diaphragm @ T₁₀.
- Esophagitis changes are max^m in the LEE (Lower esophagus end) .
- **Retzius cave** is a potential space b/w pubic bone & urinary bladder.
- RTA with pelvic injury involving bulb of penis , blood collects in superficial perineal pouch (butterfly hematoma).
- Organ of rosenmuller is a remnant of caudal part of paraovarian/epoophoron part.
- Vaginal lubrication is provided by secretions of the Bartholin's and Skene's glands.
- Volume of testes before puberty < 1.5 or 2 mL.
- Volume of testis from puberty to 20 years is 6 ml – 9 ml.
- The mean scrotal temperature is 2.5 °C less than body temperature.
- Olfactory epithelium is superior to superior turbinate of nose.
- Embryonic period is from 3rd to 8 wks post fertilisation.
- Amnion is the innermost layer facing fetus.
- Foregut is supplied by superior mesenteric artery.
- Anomic aphasia is due to lesion of angular gyrus.
- Length of medial rectus – 5.5 cm
- Length of Inferior rectus – 6 cm
- Length of lateral rectus – 7 cm
- Length of superior rectus – 7.7 cm
- Longest extraocular muscle is superior oblique.
- Syndesmosis is a type of fibrous joint.
- Bell's valve also known as anal valve.
- Largest vertebral body- lumbar region
- NOT a branch of arch of aorta --- Rt common carotid artery, Lt brachiocephalic artery.
- Pain in external hemorrhoid is transmitted through pudendal nerve.
- Singular nerve is inferior vestibular nerve.
- Vidian neurectomy is done in vasomotor rhinitis.
- 2D space between uncinate process and bulla cthmoidalis

in known as hiatus semilunaris.

- Sublingual duct that opens into submandibular duct is known as Warthin's duct.
- *Bifurcation vertebral landmarks.*
A bifurcation occurs on 4th level of each vertebral column:
C4: bifurcation of common carotid artery
T4: bifurcation of trachea
L4: bifurcation of aorta
- Aortic arch at the level of which costal cartilage- Vertbra T4, 2/3 costal cartilage .
- Arch of aorta starts and ends at: starts at t4-5 reaches T3 and ends at T4.
- Nerve supply of buccinator- facial nerve
- Pescavus is due to calcaneonavicular lig.
- Cardiac orifice of stomach is present at 7th rib.
- Optic nerve is 3rd order neuron.
- Level of Hyoid bone is C3.
- Labourer's nerve is median nerve
- Ulnar nerve is musician nerve.
- Meralgia paresthetica is entrapment of -lat femoral cut nerve.
- Test for long thoracic nerve injury - Back brush test, ask pt to back brush his hair..main hoon naa style.
- Ankle jerk- root value S1-2 and nerve checked is tibial
- Knee reflex- root value L3-4 and nerve checked is femoral.
- Subcostal line is at L1 level.
- Pubourethral ligaments is found in females and the puboprostatic ligaments in males.
- Boxer's m/s → Serratus anterior
- M/s of marriage → Medial rectus
- M/s of honeymoon → Sartorius
- Swing m/s → Pronatus quadratus
- Climbing m/s → Latissimus dorsi
- M/s of divorce → Lateral rectus
- M/s of rape or anti rape → Gracilis (gracilius)
- Tailor m/s → Sartorius
- Red m/s → Postural muscles
- White m/s → Extra ocular m/s
- Spurt m/s → Brachialis
- Shunt m/s → Brachioradialis
- Middle meningeal artery branch - Maxillary art >>> ext carotid artery.
- Dudoneum develop from - foregut & midgut both.
- Nerve root post. cutaneous .n. of thigh -- s123
- Cave of ritzius is potential space between bladder and pubic bone

- Nutrient artery of fibula.... peroneal artery
- Epithelium having absorptive property - simple columnar

PHYSIO

- Arterial blood contains 19 ml of O₂ per 100 ml of blood.
- Life of sperm in uterus is 24 – 48 hours.
- Anatomical DS is measured by **single breath N2** .
- Proximal and mid intestine absorbs: Sugars
- Middle small intestine / Jejunum : Amino acids.
- Distal SI (terminal ileum) : Bile salt & Vit. B12
- Colon (esp. caecum) : Secretes mucous and absorbs water, electrolytes and short chain FA.
- Maximum fluid and electrolytes consequences are seen after resection of ileum.
- Primary bile acids : cholic, chenodeoxycholic acids
secondary bile acids : lithocholic, deoxycholic acids.
- Fastest rate of absorption from GIT is of galactose.
Rate of absorption from GIT
Galactose (max^m) > Glucose > Fructose > Mannose
- Speed of sperm in uterus is 0.1 – 0.3 cm/hr. or 1-3 mm/hr.
- No. of Golgi tendon organs per 100 Ms fibre is 1-10
[25 Ms fibre = 1 Golgitendon organ]
- Pousielle's equation constant- ---- pi is constant....directly proportional to length, volume, rate flow, viscosity and indirectly to radius .
- DHEAs are androgens synthesized from ZR of adrenal gland.
- The ovaries have roughly 2 million primordial follicles at birth, each containing a primary oocyte. By the time of puberty, the number has dropped to about 400,000.
- Primordial follicles develop from yolk sac.
- Human ovum survive ~24 hrs after ovulation if it is not fertilized.
- In female genital tract sperms survive for 48 hours (range 1-5 days).
- Sperms moves at rate of 3 mm/min in FGT. (fructose is the principle fuel for sperm motility).
- Testosterone in male embryo is synthesized from hCG.
- Does NOT have sympathetic supply- Brain.
- 2,3 DPG is NOT influenced by - CO₂ or temperature.
- Reverse Bohr effect: Effect that occurs when lactate builds up in the blood of certain invertebrates and pH decreases, increasing the affinity of hemocyanin for O₂.
- Double Haldane effect: CO₂ transfer in placenta.
- Left shift in Cook Armeth count is seen in neutrophilia.
- *Bicarbonate* is the most important, most abundant and

primary buffer in the ECF & in plasma.

- Proteins may be considered the most **abundant** buffer in the intracellular fluid /ICF .
- Primordial follicle develops from yolk sac.
- Döhle bodies are light blue-gray, oval, basophilic, leukocyte inclusions located in the peripheral cytoplasm of neutrophils.
- *Nissle's granules/bodies* are granular material located in the intracytoplasmic ribosomes of neurons.
- Distilled water is hypotonic while 20% mannitol is hypertonic to plasma.
- Brain natriuretic peptide is degraded by - neutral endopeptidase.
- Characteristics of urine flow passing - PCT is hypotonic.
- Diabetes insipidus is the excretion of a large volume of hypotonic, insipid (tasteless) urine
- In respiratory acidosis, the kidney produces and excretes ammonium (NH_4^+) and monophosphate, generating bicarbonate in the process while clearing acid.
- Chromium tagged RBCs are used to measure red cell volume.
- RMP of smooth m/s -50mv
- Estrogen synthesis from endometrial stromal cells is upregulated by: aromatase
- Payer patches secrete -Ig A
- Lateral spiniothalamic tract carries pin prick, pain and temperature sensation.
- Normal Urine flow in man 21 ml/sec.
- Relative taste index of NaCl and sucrose is 1 .

BIOCHEM

- 21st AA -- selenocysteine
- Imino acid – selenocysteine
- Protein reversal by which a/a-proline.
- Niacin is synthesized by-tryptophan
- Phosphofructokinase deficiency causes -hemolysis
- Substrate level phosphorylation – pyruvate kinase, phosphoglycerate kinase, succinate thiokinase
- Carnithine - transport acetyl coA for fatty acid synthesis
- Mammalian taurine synthesis occurs in the pancreas via the cysteine sulfinic acid pathway.
- Essential pentosuria is a defect seen in uronic acid type I.
- Ribonuclease p is ribozyme.
- Heme synthesis enzyme ALA synthetase.
- Xanthoproteic test is shown by nitric acid. If the test is positive the proof is neutralized with an alkali, turning dark yellow.

This chemical reaction is a qualitative test, determining

the presence or absence of proteins. To quantify, it is used in another reaction, such as the Biuret, and an analysis is made by photometric spectrum.

- Ascorbic acid used for formation of hydroxylysine.
- Vitamins formed by intestinal bacteria - Vitamin K and B.
- Vitamin K epoxide cycle seen in - Conversion of proline to hydroxyproline, gamma carboxylation of bone gla protein.
- Defects in the SLC2A2 gene are a/w a particular type of glycogen storage disease called Fanconi-Bickel syndrome.
- Pyridoxin is -vit b6
- Intrinsic factor is required for absorption of vitamin B12
- Vitamin required for carboxylation -thiamine
- Vitamin required for decarboxylation -pyridoxine
- Ochronosis -alkapton is deposited
- Boiled cabbage urine is seen in tyrosinemia

GENETICS

- MHC located on chromosome is 6.
- HLA chromosome- short arm of 6
- X chromosome is bigger than Y chromosome.
- Linkage was discovered for the first time in fruit flies (*Drosophila*)
- Chromosome of Meniere's disease is 14.
- Wilson disease chromosome number-13
- Down's syndrome is a/w trisomy 21. In 95% the extra chromosome is of maternal origin, in 4% cases this extra chromosome is derived from Robertsonian translocation of 21q to another acrocentric chromosome t (13,21). In 1% cases patients are mosaic.
- Keshan's disease is d/to -selenium deficiency

PATHO

- Russell body seen in - Multiple myeloma.
- Creola bodies are seen in asthma.
- Neill-Mooser bodies are seen in Murine typhus d/to R. typhi.
- Rushton bodies are hyaline bodies found in radicular odontogenic cyst.
- Michaelis-Gutmann body are seen in Malakoplakia of urinary bladder.
- Tadpole cells are seen in pap smear of Ca Cx.
- ANCA found in Wegner's granulomatosis.
- Heart failure cells stain with hemosiderin >Prussian blue.
- Inclusion bodies are stained with Wright's stain.
- Vegetations on both sides of heart valve is seen in Libman

Sac endocarditis.

- Nutmeg liver is seen in CVC/CHF.
- Chicken wire fibrosis / Mallory body seen in liver cirrhosis.
- Vegetation in Libman sach endocarditis – Mitral, tricuspid valve, occur on both surfaces of valve leaflets, also in valve pockets. composed of fibrinoid material with fibrin n platelet thrombi. no bacteria. Multiple vegetations do not produce significant valvular deformity.
- Oval stem cell are seen in liver regeneration (Hepatic progenitor cells).
- A cadaveric donor is required for transplantation of kidney.
- When is culture done in infective endocarditis- just bfr antibiotics are started and preferably by 2-3 days of onset of symptoms and 3 samples are taken.
- M/c tumor following renal transplant-skin cancers.
- *Secondary graules* : Contain compounds that are involved in the formation of toxic oxygen compounds, lysozyme, and lactoferrin (but do not contain collagenase) .

MICRO

- Milk ring test is done for – Brucella
- Fruit shape virus is Variola.
- Bullet shape virus is Rabies.
- Fungus which multiply by budding are Cryptococcus, Candida and Sporothrix
- Plant pathogen consist of few 100 nucleobases, high complementary, circular, ss RNA, without protein coat.
- Both intra and extra nuclear inclusions are found in measles.
- Gonococci affect bulbar part of urethra first.
- Milk ring is due to- brucellosis .
- Neill-Mooser bodies are seen in Murine typhus d/to R. typhi.
- Contaminated water used for washing endoscope, will lead to infection of Mycobacterium Chelonae. Mycobacterium chelonae can cause of keratitis in soft contact lens wearers.
- Histoplasmosis is also k/as Darling d/s or Caver's d/s.
- Protozoan cysts are stored in → Low viscosity polyvinyl alcohol (LV -PVA).
- Ig which cross placenta - Ig G

PARASITO

- Crab is vector for westermanii (Lung fluke).
- Crab is intermediate host in.. Paragonimus westermani

- Mott cells are seen in the excretory part of Trypanosomes.

LAB MEDICINE

- Kernicterus is associated with- Crigler Najjar syndrome
- LDH has 5 isoforms.
- CSF sugar -2/3 of blood
- The 3rd generation TSH detection methods can detect TSH levels as low as 0.004 mU/L.

PHARMA

- Cephalosporin which causes bleeding & coagulopathy more often than other cephalosporins : Moxalactam.
- *Efavirenz* is the drug which can be given to a patient of HIV who is already on ATT.
- Centrally acting anti-hypertensives is -- Clonidine & methyldopa.
- Anti-tussive which acts by decreasing the sensitivity of stretch receptors → Benzonate.
- Binds to synaptic vesicle glycoprotein 2A (SV2A) receptor--- Levetiracetam. .
- *Rate-limiting step in synthesis of prostaglandins* -- prostaglandin synthase.
- Drug which does NOT interfere with warfarin metabolism --- Corticosteroid.
- Octreotide is NOT useful in treatment of --- Glioma.
- Automatism seen in barbiturate poisoning.
- Mechanism of action of Vigabatrin - GABA transaminase inhibition.
- Cephalosporin having side effect of bleeding-moxalactam
- Isoniazid+ pyridoxine combination is given to prevent hydrazone complex formation.
- Disulfim MOA – via aldehyde dehydrogenase
- CYP B5 : Membrane bound hemoprotein which function as an electron carrier for oxygenases.
- Keratocconjunctivitis sicca is a/w use of sulfonamides.
- M/c dose limiting Ad/e of colchicine - diarrhoea.
- Ceftriaxone can cause syndrome of pseudocholecystitis.
- Fastest acting benzodiazepine - midazolam
- Anti pseudomonal - ceftazidime , ciplox , piperacillin , imipenem , aminoglycosides..
- Drug for stress incontinence....duloxetine
- Long term of S/E of amphotericin B is hypokalemia.
- Calcineurin inhibitor drug is Tacrolimus & Cyclosporine..
- Polyenes and azoles act on fungal cell wall.
- Anti constipation drug a/w cardiotoxicity-Tegaserod

prokinetic causing MI.

- Omalizumab is anti IgE Ab, used in asthma.
- Palvizumab is used in bronchiolitis (anti-RSV).
- Cause of *C. difficile* infection - antibiotic therapy
- Drug not implicated in *C. difficile* infection - penicillin
- *Pseudomonas* infection antibiotic used is ceftazidime.

FORENSIC

- Hymen rupture due to trauma - posterior.
- Robert sign is gas in large vessel.
- Meis line seen in Arsenic poisoning.
- Total CrPC sections - 484
- Total IPC sections - 511
- Plaintiff person - plaintiff is a person who has been harmed in some way and is seeking compensation. The harm may take the form of a financial loss or physical injuries. A company may also start a lawsuit to recover damages for a loss. In some cases, the party making the claim is known as the complainant or the claimant.
- Voyeurism is also known as scotolopia and peeping tom.
- Fellatio is an act of oral stimulation of the penis by a sexual partner.
- Hymen rupture...congenital cause - rupture due intercourse or foreign body...poterolateral>post in 5 o'clock to 7 o'clock, 11-1 o'clock position due maasterbation.
- Gas in vaginatus emphysematous - N_2
- Blood in blood stains is detected by benizidine test
- Test for human blood stains - precipitin test
- The Code of Criminal Procedure, 1973 (CrPc)
- Caput succedenum indicates fetus was alive recently /2-3d back.
- Courts by which offences are triable. Subject to the other provisions of this Code,-
 - a) Any offence under the Indian Penal Code (45 of 1860) may be tried by-
 - (i) the High Court, or
 - (ii) the Court of Session, or
 - (iii) any other court by which such offence is shown in the First Schedule to be triable;
 - (b) Any offence under any other law shall, when any court is mentioned in this behalf in such law, be tried by such court and when no court is so mentioned, may be tried by.
 - (i) the High Court, or
 - (ii) any other court by which such offence is shown in the First Schedule to be triable.
- Facies types seen in hanging - la facies sympathique.
- Facies types seen in in drowning..Head low in the water,

mouth at water level..Head tilted back with mouth open - Eyes glassy and empty, unable to focus..Eyes open, with fear evident on the face.

- Hyperventilating or gasping in drowning is emphysema aquosum
- Sec 8 IPC - 8 Gender.
- CrPC 8c... Narcotics and substance abuse punishment
- labour act. prohibits labour activity of a person less than - 14yr male and 16yr female
- Juvenile delinquency act 1960 upper age limit: boy 16 and girl 18
- Robert's sign - gas in aorta
- Angel's dust - phencyclidine.
- 8c CrPC --- Punishment of narcotic & substance abuse.
- Appeal against consumer redressal can be filed in 'District Forum' (State commission).
- *Marshal's triad* is seen in explosive bomb blast injuries.
- Scalded mucosa is seen in ingestion of - H_2SO_4

PSM

- M/c food poisoning - staph
- Kit b wch lev - subcentre
- White plague term is used for TB.
- Berksonian bias is selection followed for hospital admission.
- Which is a form of self governance of block level? - Ans. Panchayat Samiti.
- Size of Aerosol is 2 - 5 microns.
- In Yellow fever till 400mtr is kept free of vector breeding.
- WHO recommends minimum number of 156 holes in mosquito net per inch square area.
- Speed of butterfly is 12 miles/hr.
- Speed of mosquito is 1.2 miles/hr.
- Speed of housefly is 4.5 miles/hr (7.2 km/hr).
- Speed of sandfly is 0.65 to 0.7 m/sec.
- Day light factor for kitchen should be $\geq 10\%$ & for living room is 8%.
- Air quality in India is controlled by central pollution control board (Ministry of environments and forests).
- Latency period to develop
 - CWP is 15-20 yrs
 - Asbestosis is 10 yrs
 - Silicosis is 10 months to 14 yrs
- Small pox vaccine - Jenner.
- Chicken cholera vaccine - Pasteur.
- Anthrax vaccine - Pasteur.

- Chicken pox vaccine – Michiaski, 1974.
- Ronald Ross - Anopheles
- Laveran – Plasmodium
- Calorie requirement in Urban is 2400 Kcal and Rural is 2600 Kcal.
- Range of PQLI is 1-100. India: 65 (Latest 43).
- HDI of India – 0.467 (max. Kerala).
- DOC for H_1N_1 is oseltamivir.
- Millenium goal 2015 to reduce IMR by? - An.s imr.. dec to 2/3rd ... mmr dec to 3/4th.
- Thermoactinomyces..... causes baggasosis .
- The range for acceptable, normal, or optimum body-mass index (BMI) for Asian populations should be narrowed to 18.5-23 kg/m²
- BMI Cutoff for asian male :
 <18.5 Underweight
 18.5 - 23.9 Healthy weight range
 24 - 26.9 Overweight
 >27 Obese Ans. 18.5-24.9
- Unmet needs for which agegrp according to national family health survey - Ans. till adolscnt
- Hepatitis E outbreak affecting 30000 people in delhi in 1955.
- Outbreak in 1994-95 in Surat - plague.
- India is in late expanding phase of demographic cycle.
- Pasteurization test used is -phosphatase test
- Insecticide used for phlebotomus - DDT
- Number of in patient beds in PHC-15
- The mode is the value that appears most
- Exponential growth occurs when the growth rate of the value of a mathematical function is proportional to the function's current value.
- Pre planning need to consider -requirmeent in community
- Malaria parsite discoverer-Charles Louis Alphonse Laveran identified the parasites that cause malaria and Sir Ronald Ross discovered how the parasite works. He also identified that the parasite is present in a particular genus of mosquito, the Anopheles. Both men won Nobel Prize for their work.
- Sanguinarine inhibits Na^+K^+ transmembrane protein function.
- Female health worker per population - 5000... and for hilly, tribal area ..3000.
- Dukoral is a monovalent inactivated vaccine It protects against travellers' diarrhea caused by E. coli as well as from cholera.
- World health day on april 7

MEDICINE

- Osborne J waves seen in- hypothermia.
- In hypocalcemia seen in ECG- QT prolonged. -
- Characteristic of Hypokalemia on ECG is U wave
- Wilson ds is a/w ---ATP7B
- Earliest ECG sign of hyperkalemia- Sine wave pattern.
- Glycogen storage disease involving GLUT 2 - Fanconi beckel
- M/c symptom of phaeochromocytoma - headache
- Pheochromocytoma-Among the presenting symptoms, episodes of palpitations, headaches, and profuse sweating are typical and constitute a classic triad.
- Primary pulmonary HTN - Loud p2, left parasternal heave, elevated jugular pulsations are seen but clubbing of fingers is NOT seen .
- Immediate treatment of Cardiac arrest is Cardiac compression > defibrillator.
- Bodies seen in parkinsonism – Lewy.
- Asterexis or liver flap in Wilson's d/s is d/to copper deposition in caudate nucleus.
- Full blown AIDS when CD4 count falls below - 200
- S4-S4 means stiff ventricle..seen in many conditions HTN,CoA ,AS, valvular lesions
- CURB-65 include
 Confusion of new onset (defined as an AMT of 8 or less), Urea >7 mmol/l (19 mg/dL), RR \geq 30 , BP < 90 mmHg systolic or DBP <60 mmHg or less age 65 or older
- Sigmund Freud born in Australia and died in London, 1939.
- Term of Alzheimer is coined in 1910.
- DOC for SIADH – Demeclocycline.
- DOC for DI – Desmopressin
- DOC for Li induced DI – Arruloride.
- No oedema is seen in SIADH because of escape phenomena by ANP c causes increase Na^+ excretion.
- Most common cause of SAH – Trauma
- Investigation of choice for pulmonary embolism is CECT angiography.
- Most commonly cardiotoxic among castor oil, mineral oil and phenophthalein is phenophthalein
- Single limb paralysis is seen in lesion of area 4
- Phaeochromocytoma spreads by..- locoregional.
- Ankylosing spondylitis does not usually present with polyarthritis and involvement of hand joints.
- MODY is -AD
- Most specific antibody for SLE - Anti Sm > dsDNA.

- Acetazolamide used in Absence seizure

SVD/SKIN

- Intraepidermal acantholysis is seen on Tzanck smear in pemphigus.
- Umbilicated vesicle is seen in Pox virus.
- Trachyonychia- 20-20 nail dystrophy
- M/c side effect of isotretinoin for acne vulgaris - Dry skin > phototoxic.
- Acanthosis nigricans most commonly a/w adenocarcinoma stomach & ovarian cancer.
- Hydradenitis suppurativa is a/w infection of - Ducts of apocrine gland.
- Chyriasis or blue pigmentation of hairs seen in gold.
- Drug causing pigmentation - minocycline

SURGERY

- Opportunistic post splenectomy infection. (OPSI) are mostly caused by pneumococci.
- Abdominal wound dehiscence (burst abdomen, fascial dehiscence) is a severe postoperative complication (on 5-7 day), with mortality rates reported as high as 45%.
- Kasai operation is done for extrahepatic biliary atresia.
- Dysphagia lusoria is due to aberrant Rt. Subclavian artery.
- Residual stone in CBD is treated by endoscopic sphincterotomy.
- First investigation in biliary tract disorder - USG
- Ureteric stone IOC - NCCT.
- M/c gas produced in intestinal obstruction --- N_2
- M/c gas produced in Clostridial infection --- H_2S
- M/c gas used to create pneumoperitoneum (in laparoscopy) --- CO_2
- M/c complication of open appendectomy - hemorrhage.
- Martorell's ulcer - hypertensive ulcers in leg.
- Costen syndrome - Temporomandibular joint pain and dysfunction.
- Zuska Disease - Periductal Mastitis.
- Rectus Sheath hematoma presents with blue skin.
- Hemobilia- Quinke's triad of upper abdominal pain, upper gastrointestinal haemorrhage and jaundice is classical. Endoscopic trans-arterial embolisation (TAE) is preferred initial t/t.
- Cryptorchidism best for diagnosis clinical examination.
- Often a submucous cleft palate is a/w a bifid or cleft uvula.
- Correction of dehydration in IHPS : using I.V. DNS (0.45% NS + 5% Dextrose + 1 meq/100 ml KCl in a dose of 2-4

meq/kg K^+).

- Gastroschisis is rt side of umbilicus while in omphalocele defect is central.
- *Deltopectoral flap* : based on perforators of internal mammary a. used for head, neck defects (cervico-facial surgery).
- M/c pedicle flap in breast reconstruction - **Latissimus dorsi flap**.
- DOC for BPH without affecting BP - tamulosin
- Balthazar CT score system - ac pancreatitis, severe if score is more than 6, computing n radin system
- Hamman sign indicate - pneumocarditis

OBG

- Best contraceptive in a newly married sweet couple - OCP
- Largest fetal diameter - mentovertical
- ARF is caused by preeclampsia.
- Weight of placenta at term - 500 gm
- Weight of uterus at term - 1000 gm
- Placenta weight is 500 gm and its ratio with fetal weight is 1:6 at term.
- Hysteroscopy not distensible - O_2
- Asherman syndrome m/c after curettage for MTP.
- Max level amniotic fluid level at 34 weeks 1 litre.
- Blood loss in an uncomplicated C-section is ~1000 ml.
- Incidence of scar rupture in previous LSCS is 0.1%.
- OC pills are started on 1st or 5th day of menstrual cycle.
- Spielberg criteria were given for ovarian pregnancy.
- Best method for ovulation - Endometrial biopsy.
- Routine method for ovulation - USG
- Antenatal hemorrhage case - Ans. abruptio placenta
- Amniotic volume at term - 800ml.
- Young girl, ovarian tumor. AFP very high - Germ cell tumour.
- Ovarian tumor with abdominal enlargement seen - Mucinous cystadenoma.
- DOC for ovarian carcinoma - carboplatin + paclitaxel
- OCP can cause carcinoma...breast & cervix carcinoma.
- Both men & women (couple) are HIV +ve. The best advice for them is condom.
- M/c symptom of tubal pregnancy - pain
- Colposcopy for cytology done at - lateral wall. hormonal -- lateral. cervical cytology -- posterior fornix
- HPV affects - top most layer / Stratum corneum
- M/c Ovarian ca - serous cystadenoma
- M/c benign ovarian ca - serous cystadenoma
- M/c malignant ovarian ca - serous cystadenocarcinoma
- M/c Ovarian germ cell tumor - dysgerminoma

- M/c rapidly growing ovarian ca-- endodermal sinus tumor
- M/c radiosensitive ovarian ca-- dysgerminoma
- M/c spread of dysgerminoma-- lymphovascular
- M/c benign germ cell tumor-- dermoid
- M/c benign ovarian tumor of pregnancy-- dermoid
- M/c malignant ovarian tumor of pregnancy-- dysgerminoma
- Mc sign of fetal demise is - Reversed diastolic flow
- Part of biophysical profile (BPP) - AFI/ NST/ foetal movement
- Vulvectomy is done in - chancroid/ warts.
- *Spiegelberg's criteria* : Helps to identify the ovarian pregnancy from other ectopics
- D&C is the m/c cause of uterine synechiae & Asherman syndrome..
- Clue cells are classically seen in Gardnerella vaginalis but c/b seen in Trichomoniasis also. Clue cells are stained by NaCl. Nugent's criteria to quantify or grade bacteria in BV.
- *The Whiff test* may be positive in up to 70% of BV patients. This test is performed by placing a drop of 10% KOH on slide.
- Gestation sac is formed 100% (completely) at β -hCG level of 2400.
- Minimum β -hCG concentration that blood serum test can detect is 5 mIU/mL.
- To detect ovulation the best method is endometrial biopsy during leuteal phase.
- Ovulation depends upon LH + FSH both.
- Vaginal sponge failure rates for women who have never delivered vaginally (nullipara) range from 9% to 16% and 32% in multipara.
- Early amniocentesis is done b/w 12 to 14 wks
- K.b. Test -KB test is used to determine the amount of mixing before giving Rh serum .

OPHTHALMO

- Orbit volume is --- 30 ml
- Eye volume is --- 6.5 ml
- *Reid base line* passes through the lowest part of the infraorbital margin and the middle of the external auditory meatus.
- *Bare orbit sign* is seen in sphenoid wing dysplasia.
- Tattooing of cornea is identified with Au (gold).
- M/c presentation of anterior uveitis - sudden onset unilateral pain, photophobia, lacrimation and blepharospasm.....

- aqueous flare-earliest sign, keratic ppt-pathognomic
- Stye is inflammation of sebaceous glands of Zeis
- NOT a feature of prodromal stage of narrow angle glaucoma - metamorphosis.
- 3rd nerve supply- inf oblique
- Corneal transplant-m/c infection herpes
- International Vision 2020 is for..cataract, refractive errors, childhood blindness, trachoma, oncocercariasis.
- Posterior staphyloma seen in -Ans. pathological myopia
- Deliriant poison is - dhatura.
- Dhatura seed looks like capsicum seeds.
- M/c intraorbital tumour in children - rhabdo in adults--- cavernous hemangioma.
- In concomitant squint, what is the relation between 1st and 2nd degree deviation- PD=SD
- Eales d/s is recurrent vit h'mgge.
- In homocystinuria dislocation of lens is inferonasal.
- In Marfan's syndrome dislocation of lens is supero-temporal.
- Sceleral buckling is done in : Retina detachment
- *Schwalbe's line* is the anatomical line found on the interior surface of the eye's cornea, and delineates the outer limit of the corneal endothelium layer..
- Blurring in underwater is d/to \downarrow refraction of cornea.
- Cholinergic amacrine cells (inner plexiform layer) can secrete Ach & GABA.
- A-waves in ERG are produced by - rods & cones.
- In retinal detachment, anterior segment examination by slit-lamp reveals fine pigmented cells/tobacco dust on the anterior face of the vitreous k/as *Shaffer's sign*. With no h/o trauma/Sx it is pathognomonic of a retinal break.
- **Angiod streaks** are d/to breach in Bruch's membrane. Seen in pseudoxanthoma elasticum, EDS, SCD, thalassemia, Paget's d/s.
- Bulls eye retinopathy is seen in hydroxy chloroquine toxicity.
- *Reid base line* passes through the lowest part of the infraorbital margin and the middle of the external auditory meatus.
- *Symblepharon* is adhesion of both bulbar & palpebral conjunctiva. It results either from d/s (conjunctival sequelae of Trachoma) or trauma. Cicatricial pemphigoid and, in severe cases, rosacea may cause symblepharon.
- Acute hemorrhagic conjunctivitis is caused by adeno 3,7.
- Cholinergic amacrine cells (inner plexiform layer) can secrete Ach & GABA.
- A-waves in ERG are produced by - rods & cones.

- Posterior staphyloma is seen in pathological myopia.
- Screening age group for trachoma 5-9 yrs.
- 20 Snowbanking seen in para planitis.
- Angiod streak is seen in pseudoxanthoma elasticum.
- Mutton fat appearance of KP's is seen in - anterior uveitis.
- Dalen fuch nodules -symp ophthalmitis
- Optic chiasma lesion produces bitemporal hemianopia.
- Plexus in corneal endothelium – annular plexus

ENT

- M/c organism acute epiglottitis- streptococcus.
- Bony damage of nasal septum seen in syphilis.
- Rhinoscleroma is caused by- Klebsiella rhinoscleromatous k/a frisch bacillus.
- Phelps's sign on CT- loss of crest of bone between carotid canal and jugular canal in glomus jugulare.
- Semicircular canals detect angular acceleration while otolith detect linear acceleration.
- M/c site nasopharyngeal ca fossa of Rosenmuller.
- Not a common cause of ant nasal septum bleed - thrombocytopenia.
- Acute necrotic otitis media is seen after measles or influenza. Caused by beta hemolytic streptococci.
- Structure in lateral wall of mastoid-. zygomatic greater wing of sphenoid
- Mc site of skull fractr- m/c bone is temporal, in that bone longitudinal 80 percent, transverse 20%, transverse more complicated.
- Lymph nodes in nasopharyngeal carcinoma -Cervical lymphadenopathy (disease or swelling of the lymph nodes in the neck) is the initial presentation in many patients,
- Suprameatal triangle lies over mastoid antrum.
- Caldwell Luc operation is done for maxillary sinus.
- Gradingo syndrome is
 - Petrositis
 - Vth CN involvement (retro-orbital pain)
 - VIth CN involvement (Lat rectus with diplopia).
- The retropharyngeal space (space of Gillette) lies behind the posterior pharyngeal wall and the pre- vertebral muscles covered by fascia.
- Surface area of round window to tympanic memb ratio 17:1
- Light house sign is seen in stage of suppuration in acute otitis media.
- Node of rouvier is lateral group of retropharyngeal nodes.
- Stylohyoid nerve supply glossopharyngeal nerve.
- Abductor of vocal cord is posterior cricoarytenoid.

- Pyriform fossa present in - hypopharynx or laryngopharynx
- In BERA, v wave denotes lesion in - inf colliculus
- Bare orbit sign is seen in sphenoid wing dysplasia.
- A Meniere's disease gene linked to chromosome 12p12.3.
- **Rhinophyma is d/to hypertrophy of sebaceous glands. Glandular form of acne rosacea.**
- During maxillary (antral) washout sudden death occurs d/ to air embolism.
- *Antral sign* on CT or *Hollman Miller sign* (anterior bowing of posterior wall of maxillary sinus) is pathognomonic of angiofibroma.

ORTHO

- Bony damage of nasal septum seen in syphilis.
- Osteoporosis m/c affect-long cancellous bone.
- Apparent lengthening is seen in stage 1 TB synovitis .
- M/c dislocation of elbow post dislocation.
- Most common fracture in elderly- # neck femur .
- Column concept of spine stability is given by Dennis.
- Internal fixation of fracture not done in - Active infection.
- Localised bony dysplasia of the femoral neck Characterised by a decreased neck shaft angle and the presence of a triangular ossification defect k/as Fairbanks triangle. Seen in coxa vara.

PEDIATRICS

- Modified ballard is used for neuromuscular maturity in preterm babies.
- Signs of hypothyroidism in neonates- unconjugated hyperbilirubinemia, prolonged neonatal jaundice.
- % of LBW - Ans 28
- 3 yr old child weighing 12 kg. What is the dose of ors. - Ans. 900ml
- Best investigation for hypothyroidism - TSH
- Hepatitis A vaccine is given at 1 year.
- Reticulocyte count of new born is 2 to 6.
- Vaccine given at 9m-measles.
- ORS stands for.....Oral Rehydration Solution
- M/c infection likely to be transmitted during parturition- CMV.
- Ballard score-This scoring allows for the estimation of age in the range of 26 weeks-44 weeks. The New Ballard Score is an extension of the above to include extremely pre-term babies i.e. up to 20 weeks...The Physical criteria These are: 1. Skin 2. Ear/Eye 3. Lanugo Hair 4. Plantar Surface 5. Breast bud 6. Genitals

RADIO

- ☉ Colon cut off sign is seen in acute pancreatitis.
- ☉ Striate vertebra is seen in hemangioma.
- ☉ Sign in total colonic aganglionosis- microcolon..
- ☉ Microcolon is seen in patients with meconium ileus; distal jejunal, ileal, or proximal colonic atresia; and megacystis-microcolonintestinal hypoperistalsis syndrome.
- ☉ Saw tooth appearance of sigmoid on barium enema - Diverticulosis.
- ☉ Test for myocardium viability-thallium 211

ANAESTHESIA

- ☉ Cheops...pain scale..is Childrens Hospital of Eastern Ontario Pain Scale. used in children.
- ☉ DISS index is used to prevent wrong fitting of central supply to machines.
- ☉ Eutactic mixture /EMLA cream is 2.5% ligno +2.5% prilo.
- ☉ Short day care surgery anesthesia used - propofol
- ☉ Drug used in local anaesthesia in hypertensive to enhance its accumulation-clonidine
- ☉ Diameter index safety system (DISS) is used to standardize connections b/w cylinders and flowmeters. (Pressure regulators). Each gas has specific attachments to prevent hook up of wrong gas.
- ☉ Complex regional pain syndrome types1 (reflex sympathetic dystrophy)...a/w ... soft tissue injury or immobilisation.
- ☉ Complex regional pain syndrome types2.....a/w well defined peripheral nerve injury.

CRITICAL CARE

- ☉ Marshall's triad includes punctate bruises, abrasions, and small punctate lacerations, all of which are typically found in an explosive bomb blast.

PSYCHIATRY

- ☉ Prophylactic dose of Li in bipolar disorder: prophylactic 0.6-0.8, therapeutic 0.8-1.2.
- ☉ 2nd generation antipsychotic- Risperidone.
- ☉ Hangover Rx - thiamine

ONCO

- ☉ Kaposi sarcoma caused by HHV-8.
- ☉ Kaposi sarcoma is of vascular origin.
- ☉ Hairy cell leukemia is d/t EBV.
- ☉ Hairy cell leukemia DOC is cladribine.
- ☉ BRCA-1 is present on 17p chromosome.

- ☉ Radial scar in breast is seen in complex sclerosing lesion or sclerosing papillary proliferation or infiltrating epitheliosis or indurative mastopathy also known as Black star breast
- ☉ Overactive bladder is seen in UTI.
- ☉ Endolymph in ear is produced by stria vascularis.
- ☉ Removal of kidney along with ureter is done in transitional cell Ca.
- ☉ M/c cancer of skin is associated with Arsenic - BCC
- ☉ Typhlectomy in Ca cervix is done upto stage Ib.
- ☉ Lorenzo oil therapy is used for adrenoleukodystrophy.
- ☉ RB gene is activated in dephosphorylated form.
- ☉ Tobacco causes ca m/c at...buccal mucosa > tongue
- ☉ Whipple's triad is seen in insulinoma.
- ☉ Jackson grading/classification is used for Ca Penis.
- ☉ Most common tumour of heart- Primary heart tumor in children is Rhabdomyoma. In Adults it is Myxoma.
- ☉ Kaposi sarcoma is seen in -HIV
- ☉ Thorium can cause -lymphangiosarcoma
- ☉ Tumor NOT seen in 1st decade of life- ameloblastoma/
- ☉ Codman triangle is seen in osteosarcoma.
- ☉ Matrix forming tumour - chondroblastoma
- ☉ Not an indication of breast conservative surgery - prior RT.
- ☉ Prognosis of Ca penis depends on -----LN

HEMATO

- ☉ Drug used for CML/tyrosine kinase inhibitor - imatinib.
- ☉ Vita B12 deficiency is a/w megaloblastic anaemia, Centrocecal scotoma, shilling's test.
- ☉ Dermatopathic lymphadenopathy is seen in mycosis fungoides.
- ☉ AML good prognostic-hyperploidy.
- ☉ Philadelphia chromosome is- t 9/22

SYNDROME

- ☉ Turner syndrome is a/w ---coarctation of aorta
- ☉ Brushfield spots are seen in Down syndrome
- ☉ Martin bell syndrome is fragile X syndrome
- ☉ Fragile X chromosome is a/w FMRP deficiency
- ☉ NAME syndrome- Nevi, Atrial myxoma, Myxoid neurofibroma, and Ephelides.

SCIENTISTS

Scientists	Role
Alexander Fleming	Discovered penicillin in 1928. Born on 6th August 1881 & death on 11th march 1955
Arnold Pick	Term Dementia Praecox was given
Charles Louis Alphonse Laveran	Identified the parasites that cause malaria
Sir Ronald Ross	Discovered how the malarial parasite works. He also identified that the parasite is present in a particular genus of mosquito, the Anopheles. Both men (he & Charles Lois) won Nobel Prize for their work
Edward Jenner	Discovered Small pox vaccine. Died jan 26 1823
Emil Kraplin	Popularized the term Dementia Praecox
Elec Jefferey	DNA profiling was 1st reported by him
James Lindt	Associated with Scurvy
Von Haff	Osmosis theory, reverse osmosis
Christian bernard	Heart transplant
Thomas Starz	liver transplant
Eric Muhe	Laparoscopy

- Dr. Thomas Starz -- liver transplant
- Dr.christian bernard-- heart transplant
- Dr. Eric muhe-- laparoscopy
- Nobel prize in physiology/medicine for 2006 was awarded to Andrew Z. Fire and Craig C. Mello for discovery of RNA interference.
- Alexander fleming died march 11th 1955
- Edward jenner died jan 26th 1823

Father of

Father of	Scientist
Modern Anatomy	Andreas Vesalius
Modern Microbiology	Loius Pasteur
Modern Toxicology	Mathieu Orfila
Clinical Toxicology	Henry James
Modern Psychiatry	Philipe Pinel (He founded humane approach for treating mentally-ill persons)

- Father of obs USG - Denis
- Father of modern toxicology ----Mathieu Orfila

